Sec. 8

THE LANCET

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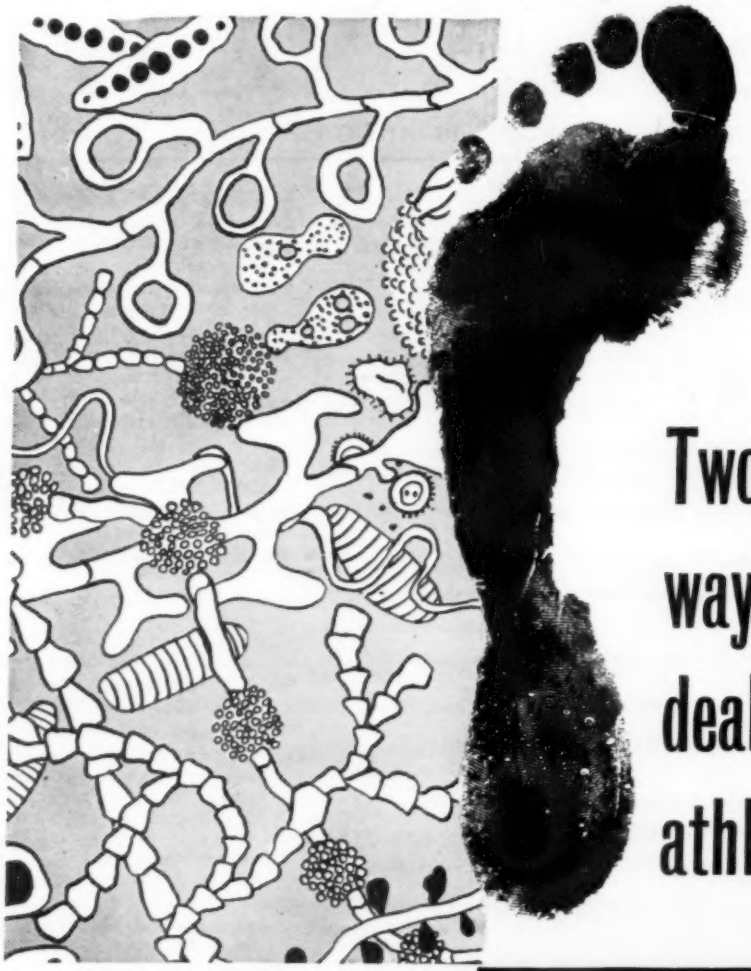

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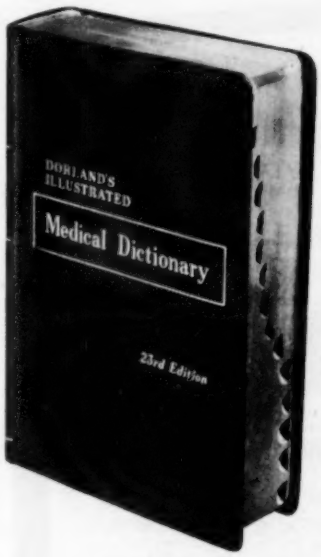

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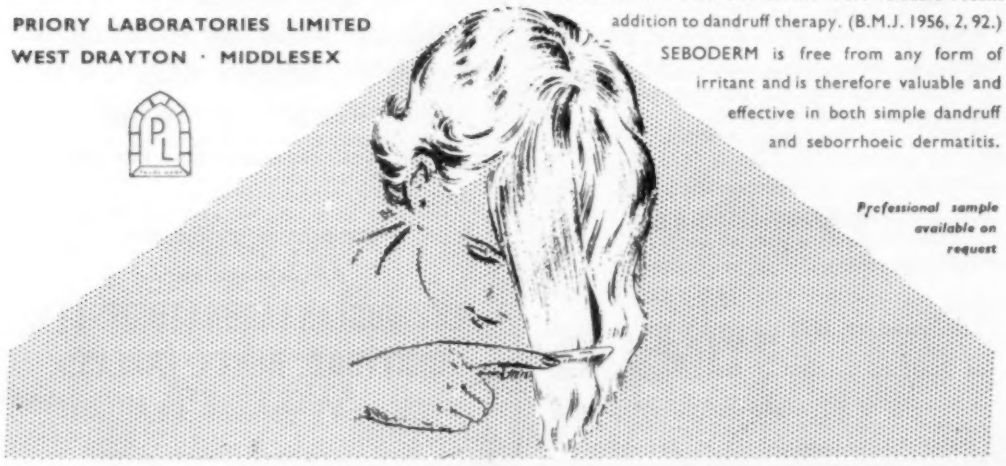

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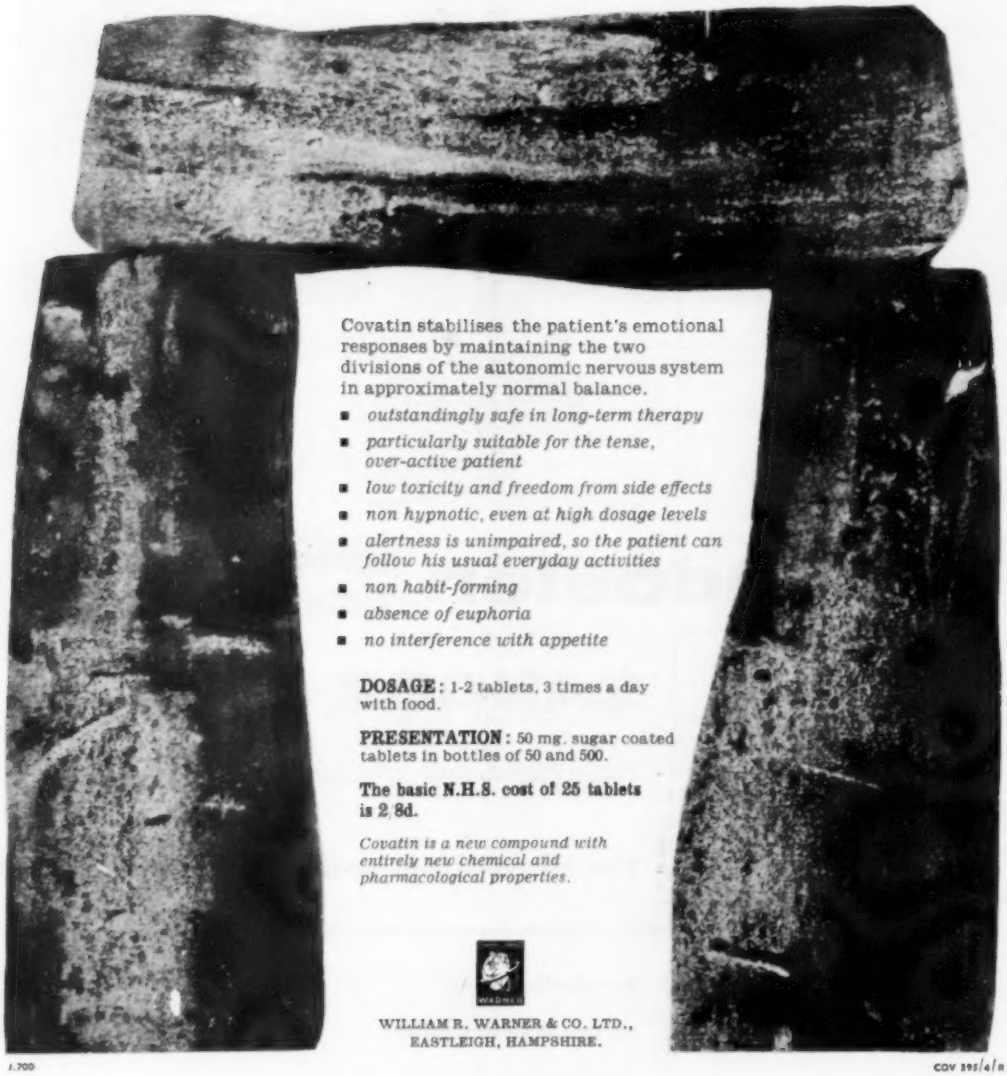

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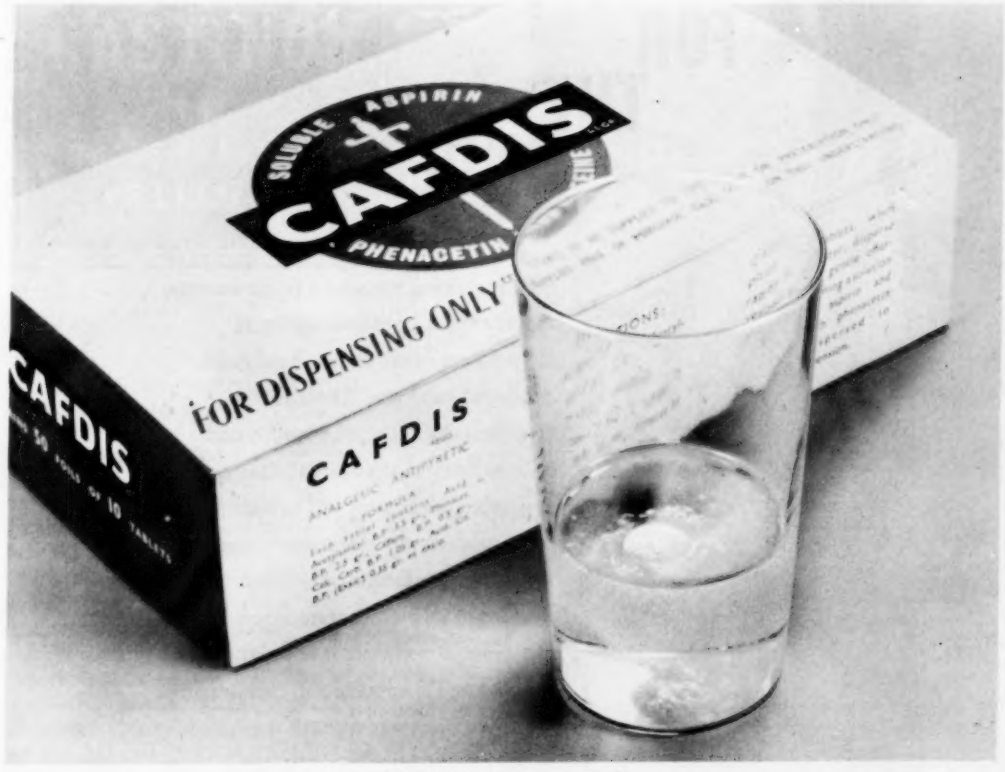

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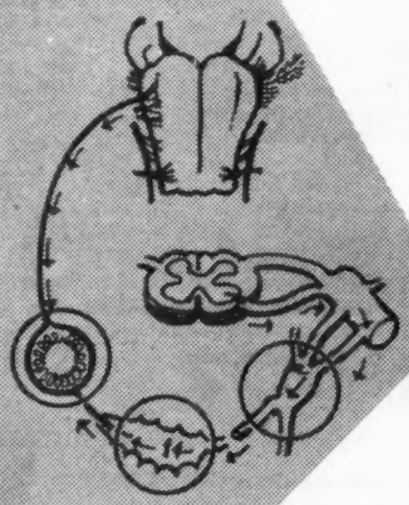

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REFERENCES:
Nature 1958, *181*, 1397; *Nature* 1958, *181*, 1717; *Lancet* 1958, *ii*, 6.

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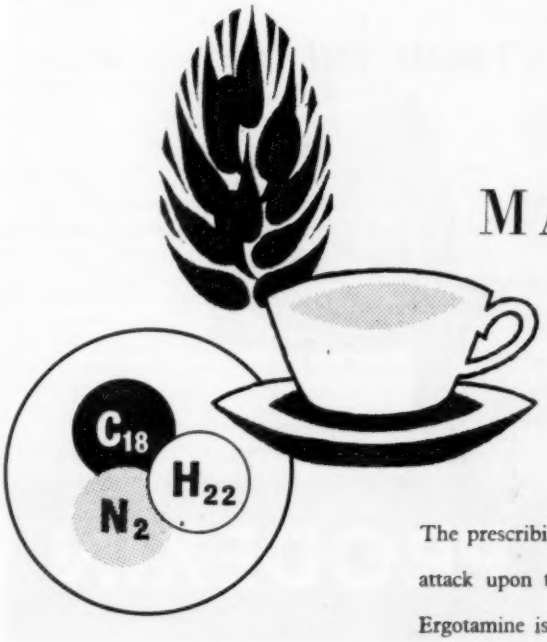

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CEREBRAL VASCULAR DISEASE IN THE LIGHT OF MODERN TECHNIQUES *

J. ST. C. ELKINGTON
M.D. Cantab., F.R.C.P.

PHYSICIAN-IN-CHARGE, NEUROLOGICAL DEPARTMENT, ST. THOMAS'S HOSPITAL, LONDON, S.E.1; PHYSICIAN, THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON, W.C.1

I PROPOSE now to consider some varieties of intracranial hæmorrhage. Extradural and subdural hæmorrhage, though both important and interesting, are self-contained subjects which have not been greatly influenced as regards either diagnosis or treatment by the developments of the past ten years. I shall therefore omit them and shall confine my attention to subarachnoid hæmorrhage and to intracerebral hæmatomas.

Subarachnoid Hæmorrhage

Since the papers of Fearnsides (1916) and of Symonds (1924), the clinical picture of subarachnoid hæmorrhage and its predominant relationship to the rupture of cerebral aneurysms have been generally recognised.

It has become customary to use the term "spontaneous" subarachnoid hæmorrhage to differentiate those cases where the bleeding into the subarachnoid space is the primary event from those in which it is secondary—for example, to head injury or to intracerebral hæmorrhage.

The clinical picture of subarachnoid hæmorrhage with its dramatically sudden onset of severe occipitofrontal headache, vomiting, shock, alteration in consciousness, and signs of meningeal irritation are familiar, and I do not propose to dwell on them. Occasional atypical cases are encountered where the characteristic bloodstained, xanthochromic fluid is found unexpectedly in a patient with less readily recognisable symptoms or is absent in cases that otherwise seem fairly typical; but by and large the clinical syndrome of spontaneous subarachnoid hæmorrhage is a very characteristic one.

Since the original papers already referred to, a number of series of cases have been published with a view to establishing the causative pathology of subarachnoid hæmorrhage. Before arteriography was available workers depended for diagnosis either on clinical judgment or on necropsy findings. The former introduces many possibilities of error. The latter inevitably gives a distorted picture since only the cases with a fatal outcome can be examined. Even at necropsy the cause of the bleeding may not be clearly established and it is generally believed that, in the process of rupturing, a small aneurysm or angioma may destroy the evidence of its own existence. It should also be remembered that an analysis of the relatively selected cases in a surgical clinic is likely to give results that are not strictly comparable with those obtained from a general hospital where the cases are unselected. It is thus difficult to obtain a wholly satisfactory estimate of the relative frequency of the many possible causes of subarachnoid hæmorrhage; but it is noticeable that the more searching the investigation, the greater is the importance attached to the rupture of some pre-existing vascular anomaly of which "berry" aneurysms constitute the great majority and angiomatous malformations a small minority.

Table I summarises the findings of a number of authors as to the relative frequency of the common causes of spontaneous subarachnoid hæmorrhage. It will be seen that with one exception upwards of 75% of proved cases are attributable to ruptured aneurysms.

Until about ten years ago the exact cause of a subarachnoid hæmorrhage may be said to have been largely of academic interest. A knowledge of the pathology might enable one to hazard a slightly more accurate prognosis; and it was, of course, important that some curable underlying condition, such as subacute bacterial endocarditis, should not be overlooked. The occasions on which one could be certain even on which side of the intracranial cavity the bleeding-point was situated were few, and more precise localisation depended on such associated findings as cranial-nerve palsies, focal fits, or evidence of local damage to the brain—e.g., dysphasia, monoplegia, or hemiplegia, which, more often than not, were absent.

TABLE I—RELATIVE FREQUENCY OF COMMON CAUSES OF SPONTANEOUS SUBARACHNOID HÆMORRHAGE IN REPORTED SERIES

Author and date	No. of cases	Mode of proof	Aneurysms (all kinds) (%)	Other causes (%)	Unknown (%)
Taylor and Whitfield (1936)	43	P.M.	77	5	18
Magee (1943)	58	P.M.	74	Not specified	
Hamby (1948)	47	P.M. 41 Op. 6	93·6	Not specified	
Hyland (1950)	55	P.M.	80	Angioma 3·8	16·2
Wolfe (1953)	62	P.M.	79	10	11
Walton (1956) (series A)	82	P.M.	72·1	15·9	12

P.M. = postmortem examination. Op. = operation.

In the years from 1925 to 1945 treatment of subarachnoid hæmorrhage could only be conservative and consisted of skilled nursing, the judicious use of sedatives and analgesics, and protracted bed rest. The only point in dispute was whether repeated lumbar puncture was advisable or not. Under these conditions it was generally recognised that the disorder carried a considerable, indeed a heavy, mortality which increased with age after 40 years. It was also recognised that death from the initial hæmorrhage usually occurred within one week of the onset of the hæmorrhage and that the dangers of a fatal recurrence progressively decreased after the first eight weeks. But precise and reliable figures were hard to come by as few workers could report on a sufficiently large number of cases under their own care, and pooled results even from the same hospital were open to obvious criticism.

Of more recent years a number of series sufficiently large and uniform to be relied upon have been reported.

In table II are set out the results of a number of inquiries

TABLE II—MORTALITY IN SPONTANEOUS SUBARACHNOID HÆMORRHAGE

Author and date	No. of cases	Mortality (%)	Period over which reckoned
Taylor and Whitfield (1936)	81	63	2 mos.
Magee (1943)	150	56	2 mos.
Hamby (1948)	130 (98 in 1st attack; 32 in subsequent attacks)	51·5	
Hyland (1950)	191	53	6 mos.
Ask-Upmark and Ingvar (1950)	138	28 43	"In hospital" Including follow-up
Wolfe (1953)	91	57	"In hospital"
Walton (1956)	312	45	"In hospital"

* The second Lumleian lecture for 1958, delivered before the Royal College of Physicians of London on April 17.

in the past ten years with regard to the mortality of subarachnoid hæmorrhage treated conservatively. It will be seen that, with one exception, they show a mortality-rate of 45–60% and we are forced to the unpleasant conclusion that at an optimistic estimate a patient with a subarachnoid hæmorrhage treated conservatively has only an even chance of being alive two months later. I doubt if it is yet generally recognised among physicians how serious is the prognosis in this condition.

Although isolated cases had been reported earlier by Dott (1933) and McConnell (1937) and other surgeons, Walter Dandy (1944a and b) was the first to make a serious attempt to eliminate cerebral aneurysms by direct surgical attack.

Although in some of his cases the aneurysm had given rise to suba chnoid hæmorrhage, he was primarily interested in the surgical treatment of intracranial aneurysms rather than that of subarachnoid hæmorrhage itself and his cases were selected for operation because the aneurysms could be localised on clinical or radiological grounds and were judged to be amenable to surgical treatment. Cerebral angiography was at this stage still in its infancy, and Dandy (1944a and b) referred to it in critical and even in disparaging terms. Dandy not only treated saccular aneurysms of the carotid artery by carotid ligation in the neck but also made a direct attack on a number of berry aneurysms situated at the termination of the intracranial portion of the carotid artery and even more distally.

In the past ten years cerebral angiography has forged rapidly ahead, and with the development of the percutaneous technique and of improved contrast media it has yielded valuable results over a wide range of cerebral disorders.

As regards subarachnoid hæmorrhage it has provided in many cases, for the first time, a means of determining with certainty during life the exact position and nature of the source of hæmorrhage, thus enabling a direct attack on the bleeding-point to be contemplated.

Reporting the results in 461 cases of subarachnoid hæmorrhage investigated during the acute stage by bilateral carotid angiography McKissock (1956) and Walsh (1956) give the following figures:

Arterial aneurysms	249 (54%)
Arteriovenous malformation	53 (11·5%)
Primary intracerebral or intracerebellar hæmorrhage	35 (7·5%)
No lesion demonstrated	124 (27%)
	461

Of the 124 cases in which no lesion was demonstrated by angiography 93 were chosen for follow-up and 31 were discarded because, for one reason or another, bilateral carotid angiography had not been performed on them. Over a period of up to eleven years the mortality in this group of 93 had been 8%, which may be favourably compared with the generally recorded mortality of about 50% during the first two months after the initial hæmorrhage and a further 20% among the survivors as recorded by Hyland (1950). It must surely follow that if the prognosis in cases showing no lesion by angiography is so much better than the average, those cases having a demonstrable lesion must carry a mortality correspondingly higher than the average.

The finding of angiomatous malformations as the cause of subarachnoid hæmorrhage in no fewer than 11% of cases (Falconer [1951] had previously found 6%) was in itself an important advance, for the natural history and surgical handling of these abnormalities are totally different from those of leaking aneurysms, and the prospect of permanent cure in cases satisfactorily operated upon is much greater since there is little, if any, liability to recurrence of the bleeding.

In a later paper McKissock and Walsh (1956) reported that the anatomical distribution of the aneurysms demonstrated was as follows:

Internal carotid artery at level of posterior communicating artery	25%	82·5%
Internal carotid artery at level of bifurcation	12%	
Anterior cerebral and anterior communicating arteries	28·5%	
Middle cerebral artery	17%	
Anterior cerebral artery (distal)	3%	
Multiple aneurysms	7·5%	
On vessels in posterior cranial fossa	6%	
Site not established	1%	

These figures, which are generally comparable to those given by others reporting the results of angiography and also those derived from postmortem studies, make it clear that the vast majority of cerebral aneurysms arise from derivatives of the carotid arteries and that they fall into three main groups—(1) those derived from the carotid artery from its point of entry into the subarachnoid space to its termination, (2) those derived from the anterior cerebral or anterior communicating arteries between the hemispheres, and (3) those derived from the middle cerebral arteries in the depth of the Sylvian fissures (fig. 7).

While aneurysms in any of these situations may give rise to subarachnoid hæmorrhage it would be surprising if structures so diversely placed were to behave identically after undergoing rupture or proved to be amenable to identical methods of surgical treatment. As we shall see, the elucidation of these questions has been one of the chief problems to which writers on the subject have paid attention in the past few years.

The first series of considerable size of cases of subarachnoid hæmorrhage from ruptured aneurysms treated surgically was published by Falconer (1950, 1951), who reported a further series of 50 in 1956. His first series consisted of 50 cases all proved by bilateral angiography to have cerebral aneurysms which had given rise to subarachnoid hæmorrhage. All were treated surgically by one or other form of carotid ligation or by direct attack on the aneurysm or by both. Falconer reported a survival-rate of 82% with a satisfactory-recovery rate of 66%, and a mortality of only 18%.

He pointed out (Falconer 1951) with apparent justification that, as his series contained a considerable number of recurrent cases, the mortality, had they been treated conservatively, would probably have been in excess of 50%. He concluded that all cases of subarachnoid hæmorrhage should be investigated as soon as possible by bilateral carotid angiography and that those in which an aneurysm was demonstrated should be operated upon forthwith. It might be contended that, from a physician's point of view, it is unnecessary to pursue the argument into greater detail; but the shortcoming of this paper as a guide to management of these cases is that a wide variety of surgical procedures in different combinations were applied to comparatively small groups of lesions which together totalled only 50, and that no clear indication is given as to the interval between the last hæmorrhage and the operation.

In his second series of 50 cases, operated on between 1952 and 1955, Falconer's results showed: survival-rate 94%, satisfactory-recovery rate 76%, mortality only 6% (Falconer 1956). It is noteworthy, however, that between the two series there had evidently been an important change in policy. Whereas in the 1951 series immediate arteriography was advocated in all cases, in 1956 the optimum time for arteriography and surgery was considered to be about the end of the first week after the hæmorrhage. This means that the mortality figures of the two series are not strictly comparable, since in that critical week there must have been a considerable number of deaths from the immediate effects of the hæmorrhage; and so the surgically treated cases represented a more selected group from which those carrying the worst natural prognosis had already been eliminated by death.

In 1953 Norlen and Barnum published a thoughtful paper

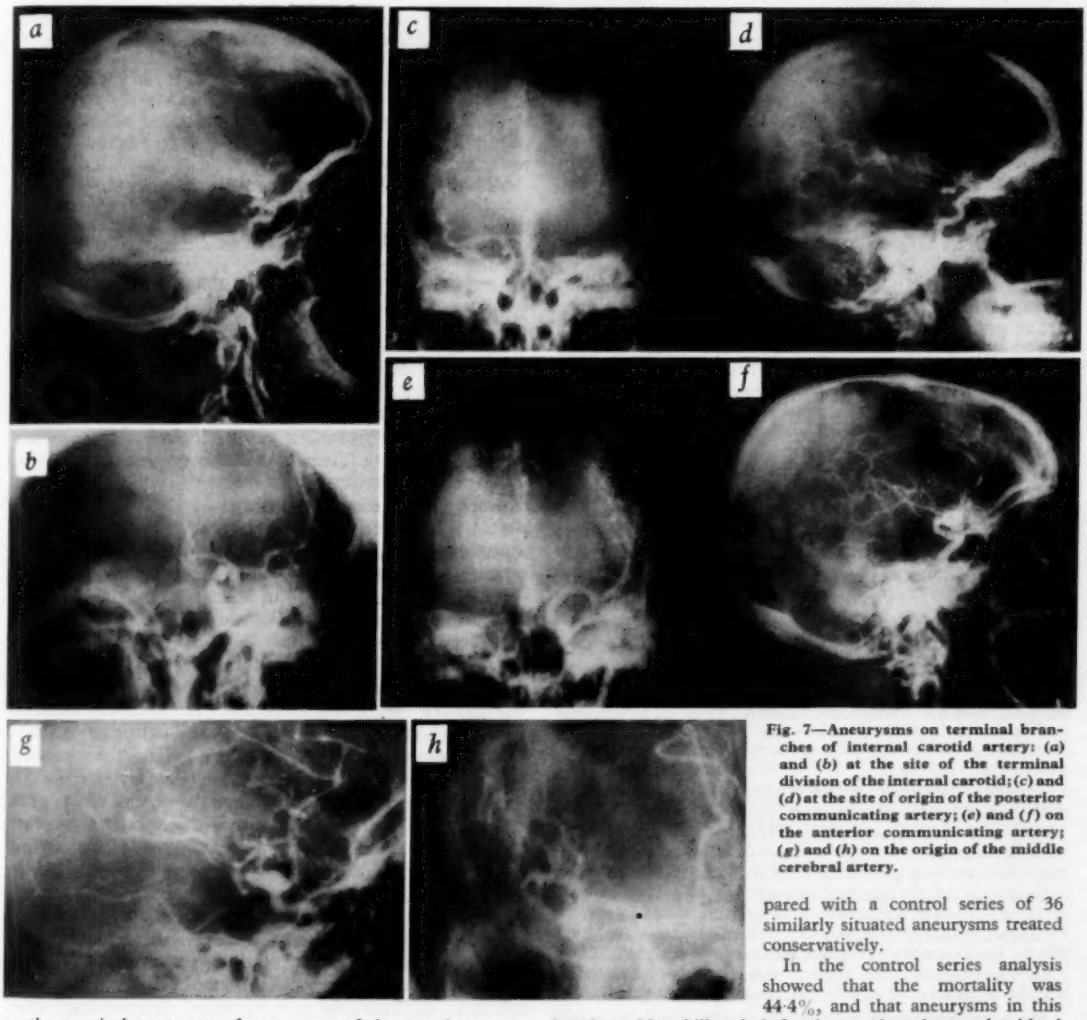

Fig. 7—Aneurysms on terminal branches of internal carotid artery: (*a*) and (*b*) at the site of the terminal division of the internal carotid; (*c*) and (*d*) at the site of origin of the posterior communicating artery; (*e*) and (*f*) on the anterior communicating artery; (*g*) and (*h*) on the origin of the middle cerebral artery.

on the surgical treatment of aneurysms of the anterior communicating artery in which they stressed the fundamental importance of the time factor and recognised that two separate problems were involved—namely, treatment in the acute stage of hæmorrhage and treatment in the free interval to minimise the danger of further hæmorrhage. Of their 26 patients, 24 had come under observation on account of a subarachnoid hæmorrhage. 24 were submitted to direct surgical attack on the aneurysm, with 3 deaths (12·5%) at or soon after operation, and another patient died eighteen months later from a further hæmorrhage.

Only 6 cases were operated on within three weeks of the initial hæmorrhage with one operative death, and of these 6 only 4 were operated on within ten days of bleeding.

In 1956 Logue published the results of a more extensive experience in the direct surgical treatment of aneurysms of the anterior cerebral and anterior communicating arteries giving rise to subarachnoid hæmorrhage. He also stressed the importance of considering separately the management of leaking aneurysms according to their anatomical situation and of relating the operative results to the interval between hæmorrhage and surgical treatment.

His series consisted of 37 cases treated by one particular type of surgical operation—i.e., proximal clipping of the anterior cerebral artery supplying the sac—and the results were compared with a control series of 36 similarly situated aneurysms treated conservatively.

In the control series analysis showed that the mortality was 44·4%, and that aneurysms in this situation seldom kill at their first hæmorrhage but tend to bleed again with fatal results during the six weeks after the initial hæmorrhage, with a peak period in the second week. Of the 20 patients who survived on conservative treatment 4 (i.e., 11% of the whole) were left with severe and lasting disabilities.

Of the 37 cases submitted to surgical treatment the overall mortality was 13·5% as opposed to 44·4% in the control series. Of the 30 survivors, 3 (i.e., 8% of the whole) were left with severe residual disabilities. Putting these figures into terms of functional recovery, of the 36 patients treated conservatively 16 were able to resume a virtually normal life, while for the 37 cases treated surgically the corresponding figure was 24 with a further 3 steadily improving at the time of publication.

From his experience of this well-controlled series of comparable cases treated by a single method, Logue concludes that at present the best treatment of bleeding aneurysms at this site (which represent 20–30% of all such cases) is to investigate them as soon as possible after the initial hæmorrhage and then to operate upon them as soon as the immediate effects of this hæmorrhage have subsided and before there has been time for a recurrence—i.e., about seven to ten days after the initial leakage.

Later in 1956 McKissock and Walsh published their results of treatment of a series of 249 cases of subarachnoid hæmorrhage resulting from verified aneurysms. They also stressed the

importance of subdividing such cases according to the anatomical site of the aneurysm and in respect of the time that had elapsed since the last hæmorrhage. While recognising that the mortality in cases operated on during the stage of acute bleeding would inevitably be high, they believed and sought to demonstrate that, even so, it was appreciably lower than it would have been in the same cases had they been treated conservatively. They also recognised that there was risk of their deductions from their results being distorted by the element of selection, and so compared their operative results not only with a comparable number of their own cases treated conservatively but with the results of other series treated conservatively.

McKissock and Walsh do not give the precise grounds on which patients were selected for surgical or conservative treatment but state that the choice was largely determined by the date at which the patient was admitted—i.e., whether before or after the date on which a more active policy was embarked upon.

They established a routine procedure for cases admitted for subarachnoid hæmorrhage. Provided that the patient successfully withstood compression of each common carotid artery in turn for ten minutes, bilateral carotid angiography was carried out. In the event of an aneurysm being demonstrated, the appropriate operation according to its site was carried out immediately. For the purpose of assessing the operative results the patients were divided into three categories according to their clinical condition, on admission in the case of those treated conservatively, and at operation in the case of those treated surgically:

Category A.—Comprised patients in danger of dying in the immediate future from the hæmorrhage causing admission. This included all cases in coma and semicoma and those with severe neurological signs.

Category B.—Comprised patients who had completely or partly recovered from the results of the hæmorrhage leading to admission but were within a period of eight weeks from it and so were to be considered in considerable danger of a recurrent and possibly fatal hæmorrhage.

Category C comprised patients admitted more than eight weeks after the hæmorrhage and who were thus at only moderate risk of a recurrence (20% according to Hyland's [1950] figures).

Comparing the results of conservative and operative treatment in these three categories, their results were as follows:

Category A.—In 43 cases treated conservatively the mortality was 90%. In 52 cases treated surgically the mortality was 65·5%.

Category B.—In 48 cases treated conservatively the mortality was 37·5%. In 72 cases treated surgically the mortality was 12·5%.

Category C.—In 17 cases treated conservatively the mortality was 6%. In 17 cases treated surgically the mortality was 23·5%.

Studying these figures critically one notices that the operative mortality for cases in Category A was 65·5%, compared with 50–60% in published series of subarachnoid hæmorrhage of all types and 90% in McKissock and Walsh's control series of cases in the same category. Operation under these circumstances can therefore only be justified on the assumption that the expected mortality for cases falling into category A if treated conservatively is much higher than the average for all subarachnoid hæmorrhages and that the mortality-rate of 90% in McKissock and Walsh's control series is truly representative. To me these assumptions seem reasonable but not everyone will agree, and the desirability of operating at the height of hæmorrhage remains sub judice.

As regards category B, the operative mortality of 12·5% as compared with that of 37·5% in the control series and the 50–60% overall mortality in published cases of subarachnoid hæmorrhage is convincing and is in conformity with the results of Norlen and Barnum (1953) and of Logue (1956) in respect of one particular group of aneurysms—namely, those arising from the anterior communicating or anterior cerebral arteries.

As regards category C, in reference to their mortality of 23·5% in 17 cases, McKissock and Walsh explain that the 4 deaths resulted from recurrent hæmorrhages at two years (1), eighteen months (2), and six weeks (1) after simple carotid ligation and that there were no deaths from the immediate effects of operation. They no longer consider carotid ligation alone to be adequate treatment for such cases.

Considering their material from the point of view of functional results, as well as survival, McKissock and Walsh point out that of 108 patients treated conservatively 51 (46%) survived, of whom only 1 was severely disabled, whereas in the 141 cases treated surgically 94 (67%) survived but 16 were severely disabled.

McKissock and Walsh, using the same clinical categories, then broke down their material on the basis of the anatomical site of the aneurysms, different surgical techniques being employed in respect of aneurysms in different sites. In subdividing the cases into so many subsections the numbers naturally become much smaller and conclusions more open to error, but these workers conclude that group for group those treated surgically showed a lower mortality than those treated conservatively.

Certain conclusions can legitimately be drawn from these various contributions. Firstly, subarachnoid hæmorrhage treated conservatively carries a grievous mortality. Secondly, active treatment can be logically applied only after an accurate diagnosis has been made and this involves bilateral carotid angiography, which should be carried out as soon as possible. Thirdly, those cases within eight weeks of their hæmorrhage are, in the absence of some special contraindication, best treated by surgical means either by direct attack on the aneurysm or by some variety of carotid ligation. Fourthly, if more than eight weeks have elapsed since the last hæmorrhage, conservative treatment is usually to be preferred to surgical treatment. The question of whether surgical treatment is indicated during the phase of acute hæmorrhage remains for the future to decide. It should be remembered that in none of the series cited was artificial hypothermia generally employed. It is now possible, under hypothermia, to cut off the cerebral circulation entirely by clamping the three great branches of the arch of the aorta for up to ten minutes without inflicting lasting damage on the brain; and accordingly it seems almost certain that, within the next few years, further evidence will be forthcoming in favour of early surgical intervention. Indeed, in a recent paper Botterell et al. (1958) have already described a series of 97 cases of cerebral aneurysm operated upon under artificial hypothermia with compression when necessary of both carotid and both vertebal arteries. Of these, 64 were operated upon within seven days of the occurrence of subarachnoid hæmorrhage, with only 19 deaths (30%).

Intracerebral Hæmorrhage

Localised hæmorrhage into the substance of the brain, conveniently referred to as an intracerebral hæmatoma, broadly speaking occurs under two widely different circumstances:

(1) By rupture of some pre-existing localised vascular anomaly such as an aneurysm or an angiomatous malformation.

(2) By rupture of an atherosclerotic vessel in a patient suffering from generalised arterial degeneration and usually from hypertension.

The second group is the one that raises the more complex questions of diagnosis and treatment.

INTRACEREBRAL HÆMATOMAS RESULTING FROM RUPTURED ANEURYSMS

The rupture of a cerebral aneurysm commonly gives rise to a subarachnoid hæmorrhage. When, however, the aneurysm is buried within the substance of the brain, as is not uncommon in those arising from the anterior or middle cerebral arteries, some and occasionally all of the shed blood ploughs up the surrounding brain tissue and

gives rise to an intracerebral hæmatoma, often of considerable size.

This complication is frequently encountered in the surgical treatment of subarachnoid hæmorrhage, and its presence can often be suspected from the clinical picture of rapidly or slowly developing signs of a space-occupying lesion with papillœdema and other signs of a sustained increase of intracranial pressure and confirmed by the shift of the cerebral arteries revealed by angiography.

It is generally agreed that the presence of a massive intracerebral clot in cases of subarachnoid hæmorrhage is a further indication for surgical intervention at the appropriate time.

INTRACEREBRAL HÆMATOMAS RESULTING FROM ANGIOMATOUS MALFORMATIONS

Intracerebral hæmatomas arising from leaking or ruptured angiomatous malformations present a somewhat different problem. They commonly occur in healthy young adults or adolescents and usually develop somewhat more slowly and less catastrophically than those due to ruptured aneurysms. They may or may not have been preceded by events suggestive of a subarachnoid hæmorrhage or of some space-occupying cerebral lesion—for example, by fits or signs of focal brain disease. According to MacKenzie (1953) 30% of angiomatous malformations present with symptoms of hæmorrhage either subarachnoid or intracerebral or a combination of the two.

The diagnosis of an intracerebral hæmatoma of this type depends upon the clinical findings of a rapidly developing expanding intracranial lesion in an otherwise healthy person, especially if additional features suggestive of hæmorrhage are present. The diagnosis is confirmed by angiography which, in addition to showing evidence of displacement of the cerebral vessels, reveals the characteristic features of the causative lesion.

Such hæmatomas should be treated surgically, at the earliest opportunity, by evacuation of the clot and excision of the angiomatous malformation if this is possible—which it usually now is thanks to the pioneer work of Olivecrona and Riives (1948). The recovery in such cases is usually gratifying in the extreme, as the following case illustrates:

Case 7.—A healthy postman, aged 30, had probably had a fit after a drinking bout when about 18 years of age. From that time he was liable to occasional headaches, but in other respects remained well until three weeks before admission when he suddenly developed a severe frontal headache and within a few seconds was aware of weakness of his left leg. This within a few minutes developed into a complete left hemiplegia. There was no disturbance of consciousness or aphasia but he had retention of urine for five days.

On examination three weeks later he had a severe left hemiplegia but slight voluntary movement was now present at hip and shoulder. The cerebrospinal fluid (C.S.F.) was yellow and under slightly increased pressure. The E.E.G. showed abnormal slow waves in the anterior part of the right hemisphere. A right carotid angiogram revealed a small angioma, just anterior to the central sulcus, deriving its blood from the hypertrophied right anterior cerebral artery. At operation a small angiomatous malformation was found and excised, and an intracerebral hæmatoma was encountered and evacuated leaving a ragged cavity in the brain 5 cm. in depth and 5 cm. in anteroposterior extent.

The patient made an uninterrupted recovery, and five years later his only remaining disability is slight weakness of dorsiflexion of the left foot.

INTRACEREBRAL HÆMATOMAS RESULTING FROM CEREBRAL VASCULAR DEGENERATION WITH HYPERTENSION

Massive intracerebral hæmorrhage in patients suffering from diffuse vascular disease with hypertension is a common and usually a terminal event. In most such cases the hæmorrhage bursts through into the ventricular cavities or on to the surface of the brain, and the bleeding continues until the patient dies. But not all such patients die in the first attack, for evidence of old intracerebral hæmorrhages is often seen at necropsy. Some live on, with varying degrees of disability, until another stroke dispatches them or until they die from some other cause; and they may survive for a long time.

In the past such patients were considered to be beyond human aid and an atmosphere of pessimism hung over their misfortunes, for it was only a matter of time before some further catastrophe overwhelmed them. But today some cases of hypertension can be cured and others can be controlled, and the question therefore arises as to whether anything surgical can be done to mitigate the consequences of such a lesion in patients who survive the initial disaster.

The first problem is clearly that of recognising the presence of an intracerebral hæmatoma, which is by no means easy. The differential diagnosis is usually from cerebral softening through infarction.

The patient is commonly a middle-aged or elderly person with the usual features of diffuse arterial disease with hypertension. The onset is often ingravescent, neither as dramatic as with the usual massive hæmorrhage nor as silent as with a thrombosis. Headache is usually severe and depression of consciousness is the rule. There may be bradycardia. These lesions are commoner in the posterior parts of the hemisphere, so the local signs usually include hemianopia and sensory disturbance as well as hemiplegia. Where the major hemisphere is involved severe dysphasia is the rule. After a few days, when a patient with an uncontrolled hæmorrhage is likely to have died and one with a massive softening to be improving, the patient with an intracerebral hæmatoma is still sinking into deeper coma, and papillœdema and other signs of increased intracranial pressure may make their appearance. The C.S.F. is under increased pressure and often xanthochromic and may be lightly bloodstained. Untreated, the patient either expires in coma in the second or third week of his illness or gradually struggles back to a normal level of consciousness and survives with a varying degree of damage to body and mind.

If an intracerebral hæmatoma is suspected its presence can often be confirmed by X-ray examination of the skull, which may show the characteristic shift of the pineal shadow away from the side of the hæmatoma. Alternatively an air ventriculogram may be needed to demonstrate the presence of an expanding intracranial lesion and the hæmatoma may be encountered in performing it.

Surgical evacuation of such hæmatomas has been reported in the literature at intervals since the first was reported by Cushing in 1903, and others later by Russell and Sargent (1909) and by Penfield (1933). But the presence of generalised arterial disease and hypertension has more often been regarded as a contraindication to surgical intervention.

In 1941 Furlow et al. reported 5 cases of intracerebral hæmatoma evacuated surgically, of which 3 were secondary to hypertension. They considered that operation was justified where improvement failed to occur with conservative measures, where symptoms and signs of raised intracranial pressure made their appearance, and where the general condition of the patient's cardiovascular system was not so serious as to contraindicate it. The ætiology and symptoms of intracerebral hæmatoma were fully reviewed by Jewesbury in 1947. In

1953 Diana Beck reported on 6 cases of intracerebral hæmatoma treated by evacuation, of which 5 were associated with moderate or severe arterial hypertension. In 1957 Gurdjian and Webster reported 11 cases operated upon, of which 6 were in patients over 50 years of age; and of these 6 patients 4 were hypertensive. Kelly (1958) has recently reviewed the clinical features of 34 cases, many resulting from hypertension, with especial reference to the results of surgical evacuation of intracerebral clots.

I have come to the conclusion that surgical treatment has an undoubted part to play both as a life-saving measure and as means of minimising the residual disability in certain selected cases of intracerebral hæmorrhage resulting from hypertension in atherosclerotic subjects.

Case 8.—A business man of 48 had been known for some years to be hypertensive, and four months previously had suffered from transient hæmaturia. Six days before admission, while abroad, he woke with severe headache and nausea. He became confused and incontinent and developed dysphasia and a right hemiparesis. Within four hours he had become semicomatose and was admitted to a hospital from which he was transferred to the National Hospital two days later.

On examination he was drowsy but could be roused sufficiently to obey simple commands. He was dysphasic, had a right homonomous hemianopia and a virtually complete right hemiplegia with considerable sensory loss. The optic fundi showed bilateral papillœdema. His heart was enlarged, blood-pressure 170/120 mm. Hg; his urine contained considerable albumin. X-ray examination of the skull showed the pineal body deviated towards the right, and ventriculography showed a large expanding lesion in the left temperoparietal region. From this, old blood was withdrawn, and at operation a large intracerebral hæmatoma was evacuated.

He made a steady and uninterrupted recovery. On discharge from hospital six weeks later he was fully alert, his papillœdema had subsided, and his right-sided weakness and sensory disturbance and dysphasia had almost disappeared. There was still a partial hemianopia and some mental impoverishment.

During the next two years he continued to improve and led an active life at home, although he was not able to return to business. He then suffered a recurrence of his headache with return of his dysphasia and right hemiparesis, but without depression of consciousness or other signs of increased intracranial pressure. His blood-pressure was 180/140 mm. Hg. He again improved, this time spontaneously, and left hospital little altered by his second attack except for further reduction of his mental capacity. Seen in recent weeks, nearly four years after his initial hæmorrhage, his condition remains much the same.

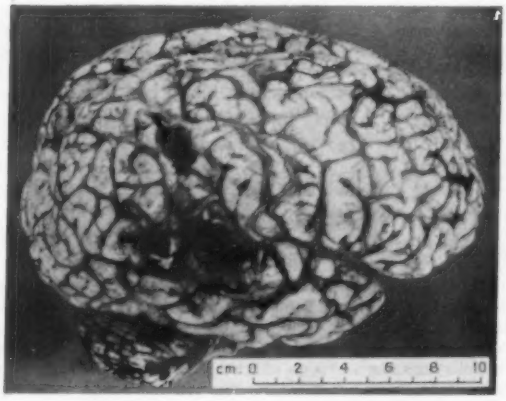

Fig. 8—Surface view of the right hemisphere in case 9, showing old bloodstaining of the pia mater over the site of evacuation of an intracerebral hæmatoma.

Case 9.—A university lecturer, aged 52, had been known to be severely hypertensive for some years, and over the course of ten years had experienced several hæmatemeses from a pyloric ulcer. He was right-handed. Three weeks before admission he had experienced sudden numbness on the left side of his face with clumsiness of his left hand, which had cleared up in two or three days. Two weeks later he developed weakness of his left arm and leg which rapidly progressed to a complete hemiplegia with increasing drowsiness and severe headache.

On examination he had a severe left hemiparesis with sensory loss and a left homonomous hemianopia. His fundi showed advanced arterial changes, his heart was enlarged, and his blood-pressure 260/160 mm. Hg. X-ray examination showed shift of the pineal body to the left, and in attempting ventriculography a blood clot was encountered by the cannula in the right posterior parietal region. As much blood as could be withdrawn was aspirated. Temporary improvement followed, but as this was not maintained a bone flap was turned down four days later and 20 ml. of solid clot was evacuated.

From this time his cerebral condition steadily improved, in spite of a further gastrointestinal hæmorrhage sufficiently severe to demand transfusion. On discharge two months after admission he was ambulant with a diminishing hemiparesis and hemianopia, and six months after his stroke he was able to return to light duties in his college. His blood-pressure remained in the region of 250/150 mm. Hg.

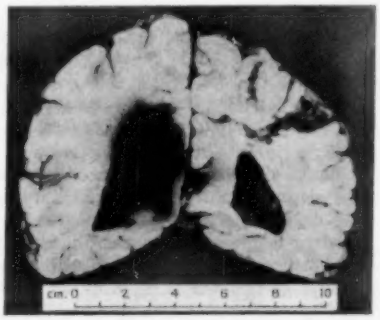

Fig. 9—Coronal sections of the hemispheres in case 9, showing a ragged cavity in the right hemisphere from which a hæmatoma had been evacuated, and a massive recent hæmorrhage into the left hemisphere.

Approximately a year after his first stroke he suffered a second. This came on while he was in bed and was heralded by disturbance of speech. By the time he was readmitted to hospital he could be roused only with difficulty and was severely dysphasic. He again had a hemiplegia, but this time it was on the right side. He gradually sank into coma and died five days after readmission.

Necropsy showed evidence of advanced atherosclerosis with cardiomegaly. The right cerebral hemisphere showed old bloodstaining under the pia in the right parietal region which was in contact with a well-healed surgical flap in the dura mater and skull. An incision in the cortex led to a narrow, ragged cavity in the walls of which there was old bloodstaining. The corresponding region of the left hemisphere was occupied by a large recent hæmorrhage which had burst through into the lateral ventricle (figs. 8 and 9).

In evaluating these and similar cases we encounter the old difficulty that no-one can say with certainty what would have happened had the patients not been subjected to operation. From experience of similar cases I think it is very unlikely that either of those two patients would otherwise have survived the initial stroke, and I am even more certain that if they had been treated conservatively the neurological damage, had they survived, would have been greater. Whether the prolongation of life in these cases was desirable or not is a matter of opinion. They have been selected for reference because in each case the ultimate prognosis was as bad as it could be, and

to many would have constituted a contraindication to any form of surgical treatment.

Conclusions

I have now completed my review and it remains only to draw some general conclusions from it. I hope it has been shown that modern surgery and a variety of technical procedures have been brought to bear significantly on the problems of cerebral vascular disease. For many years this subject has been at an impasse which has engendered an atmosphere of fatalism and inertia. Today there are signs of advance in a number of directions and an attitude of passive acceptance is giving place to one of active inquiry and experiment. Although at present modern methods of treatment may only touch the fringe of the problem, it is a growing fringe and every attempt to enlarge it should be encouraged.

This will not be easy, for the idea that cerebral vascular disease is exclusively a medical disorder is deeply ingrained in most of us. As physicians we instinctively hesitate to precipitate our patients into the hazards of surgery, the more so in a condition where the initial symptoms we observe are so often both mild and transient. A more progressive attitude will give rise to administrative problems. The correct handling of cases of cerebral vascular disease will come to depend more and more upon accurate diagnosis. This in its turn will necessitate the use of diagnostic procedures which can be carried out only in suitably equipped hospitals which have a highly trained specialist staff available at all times. It must, therefore, be expected that a steadily increasing number of cases of cerebral vascular disease will have to be transferred, often at short notice, to specialised centres for investigation and treatment. It is only at such centres that new methods can be tested under satisfactory conditions and advances in treatment achieved. Mistakes will inevitably be made; but, bearing in mind the outcome of conservative treatment, we cannot afford to be either timid or complacent.

I wish to thank my hospital colleagues for permission to refer to the records of patients under their care; Dr. William Blackwood and Dr. James Bull for their help in providing pathological and radiological material; and the authorities of the University of California through whose generosity I was afforded the leisure and the facilities without which it would have been difficult to prepare these lectures.

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ANTIBODY RESPONSE FOLLOWING INTRADERMAL OR ORAL ADMINISTRATION OF FORMALINISED POLIOMYELITIS VACCINE

JOHN H. CONNOLLY
M.B. Belf.
TUTOR

GEORGE W. A. DICK
M.D., D.Sc. Edin., F.R.C.P.E.
PROFESSOR OF MICROBIOLOGY

with the technical assistance of

D. L. CORKIN

From the Department of Microbiology, the Queen's University of Belfast

INTRADERMAL vaccination with formalinised poliomyelitis vaccine has been used over the past three years in Denmark, where an estimated 91% of the population between the ages of nine months and forty years have received two doses (von Magnus 1957). Recently Sigurdsson, Gudnadottir, and Petursson (1958) reported their experience with this method in Iceland. Since only about one-third the quantity is required for the intradermal as compared with the intramuscular route, its use is important if vaccine is in short supply. This paper records an investigation of the efficacy of the intradermal method in young children.

Numerous observations have shown that oral administration of certain toxoids or suspensions of killed bacteria can stimulate antibody production (Wilson and Miles 1955). Although this method is far less efficient than parenteral administration, we also decided to attempt

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immunisation by mouth with killed poliomyelitis vaccine since this is simple.

Materials and Methods

British poliomyelitis vaccine 'Polivirin' manufactured by Glaxo Laboratories was used. This contains formalinised Brunenders, MEF_1, and Saukett strains of polioviruses. The methods of administration were:

Intradermal.—Two doses, each of 0·3 ml. of vaccine, were given at four weeks' interval. Each dose was halved so that two injections were given into the flexor aspect of each forearm.

Oral.—Two doses, each of 5 ml., were given in milk at four weeks' interval.

Intramuscular.—Two doses, each of 1 ml., were given at four weeks' interval.

In the first trial, blood samples were taken on the day of vaccination and two weeks later. Further blood samples were obtained four weeks after the first dose and four weeks after the second dose. In the second and third trials blood samples were obtained on the day the first dose of vaccine was given and again four weeks after the second dose.

Tissue-culture techniques and virus-neutralisation tests were similar to those described by Dane, Dick, Connolly, Fisher, and McKeown (1957). Children were considered to have no demonstrable antibody when a 1/4 dilution of sera failed to neutralise 100 TCD_{50} of poliovirus. Sera were not titrated beyond a dilution of 1/512. Virus-isolation techniques were similar to those described by Dick, Dane, Fisher, Connolly, and McKeown (1957).

Results

Children of five years of age and under were selected for study since in Northern Ireland they are the age-group most susceptible to paralytic poliomyelitis. In the first trial, during May, 1957, 7 children were vaccinated intradermally and 7 others received vaccine by mouth. As a control, a further 8 children were vaccinated intramuscularly. In the second trial, in November, 1957, 15 children received vaccine intradermally, and in the third trial in January, 1958, another 30 were vaccinated intradermally. The age distribution and sex of these children are shown in table I.

Intradermal Vaccination

We first studied children who before vaccination were devoid of antibody to all three poliovirus types. The antibody response of these triple-negative children four weeks after the second intradermal dose is shown in table II.

It will be seen that 3 children devoid of antibody before vaccination remained so and that no child developed demonstrable type-1 antibody.

We next studied the antibody response in children who were initially devoid of antibody to one of the three poliovirus types. The antibody response four weeks after the second intradermal dose is shown in table III and fig. 1.

TABLE I—THE AGE DISTRIBUTION AND SEX OF THE CHILDREN IN THE THREE TRIALS

Route of administration of vaccine	No. of children in each age-group					Sex		Total
	1–2	2–3	3–4	4–5	5–6	M	F	
Intradermal	12	24	5	8	3	30	22	52
Oral	1	2	3	1	0	4	3	7
Intramuscular	0	4	2	1	1	2	6	8

TABLE II—THE ANTIBODY RESPONSE 4 WEEKS AFTER TWO INTRADERMAL DOSES OF VACCINE IN CHILDREN INITIALLY DEVOID OF ANTIBODY TO ALL 3 POLIOVIRUS TYPES

No. of children without antibody to any poliovirus type	No. of children with antibody response to			No. of children without antibody to any poliovirus type after vaccination
	type 1	type 2	type 3	
5	0	2	2	3

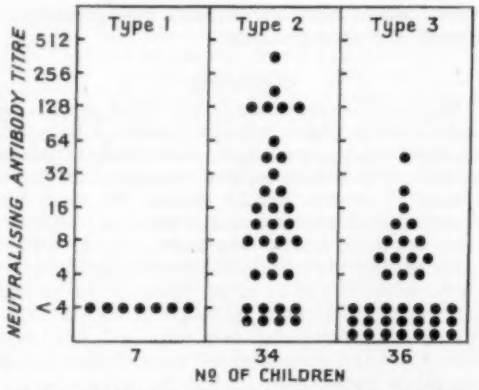

Fig. 1—The antibody response 4 weeks after two intradermal doses of vaccine in children initially devoid of antibody to 1 of the 3 poliovirus types.

It will be seen that, again, no child produced any demonstrable type-1 antibody. The proportion of children producing type-2 antibody was highest. The number of children in this age group who were initially devoid of type-1 antibody is small, possibly because of an epidemic of type-1 poliomyelitis in Northern Ireland in the summer of 1957.

The antibody response four weeks after the second intradermal dose in children who possessed naturally acquired antibody at the time of vaccination is shown in table IV and fig. 2.

It will be seen that in most cases the pre-existing antibody is boosted to higher levels by intradermal vaccination. In 3 children the type-1 antibody was not boosted, in 2 the type-2 antibody was not boosted, and in 1 the type-3 antibody was not boosted.

Of the control group of 8 children, 5 had no type-1 antibody and 1 had no antibody to any of the three poliovirus types. Four weeks after the second intramuscular dose of vaccine only 1 child had not produced any type-1 antibody, while all children of this group showed a type-2 and type-3 antibody response.

TABLE III—THE ANTIBODY RESPONSE 4 WEEKS AFTER TWO INTRADERMAL DOSES OF VACCINE IN CHILDREN INITIALLY DEVOID OF ANTIBODY TO ONE OF THE 3 POLIOVIRUS TYPES

Antibody type	No. of children without antibody	No. of children developing antibody	Percentage antibody response
1	7	0	0
2	34	26	76
3	36	15	42

TABLE IV—THE ANTIBODY RESPONSE 4 WEEKS AFTER TWO INTRADERMAL DOSES OF VACCINE IN CHILDREN ALREADY POSSESSING ANTIBODY

Antibody type	No. of children possessing antibody	No. of children showing booster response	Percentage antibody response
1	45*	37	93
2	18†	9	82
3	16‡	14	93

* Five had a prevaccination titre of 512 or more and were excluded.
† Seven had a prevaccination titre of > 512 and were excluded.
‡ One was excluded since insufficient serum was obtained for estimation of type 3 antibody titre.

TABLE V—THE ANTIBODY RESPONSE 4 WEEKS AFTER TWO ORAL DOSES OF VACCINE.

No. of children given oral vaccine	No. of children with antibody response to			No. of children without antibody response to any poliovirus type
	type 1	type 2	type 3	
7*	1	3	1	4

* A fourth sample of serum was not obtained from one child.

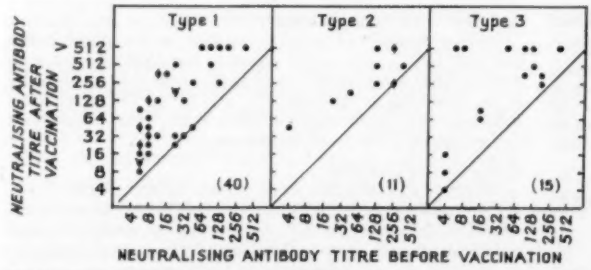

Fig. 2—The antibody response 4 weeks after two intradermal doses of vaccine in children already possessing antibody.

Oral Administration

The antibody response in 7 children who were given two doses of vaccine by mouth is shown in table v and fig. 3.

3 children had no antibody to any of the three poliovirus types before receiving vaccine and all failed to develop antibody. The number of children responding to type-2 was greater than the number who responded to either type-1 or type-3.

After each oral dose of vaccine fæcal samples were collected for ten days to exclude coincidental natural poliomyelitis infection. Because live virus was not detected, it was concluded that the antibody responses in this group were due to the vaccine. Children who failed to respond to intradermal or oral administration were later vaccinated intramuscularly.

Discussion

In children devoid of antibody to all three poliovirus types there was a poor response to intradermal vaccination (table II). This contrasts with the findings of von Magnus (1957) who in one trial showed that, of 6 children devoid of antibody to all three poliovirus types, 4 developed type-1 antibody and all developed type-2 and type-3 antibodies after two doses of 0·2–0·3 ml. of vaccine at four weeks' interval. Salk (1955) has shown that the antibody response to vaccination is less in children who are initially devoid of antibody to all three poliovirus types than in those who at the time of vaccination possess antibody to one or more poliovirus types.

Again our results show a much poorer antibody response than those of von Magnus (1957) in children who at the time of vaccination were devoid of antibody to any one of the three poliovirus types (table III and fig. 1). In the Danish trial of children initially devoid of antibody to one poliovirus type, 21 out of 30 developed type-1 antibody, all of 32 developed type-2 antibody, and 34 out of 35 developed type-3 antibody. Sigurdsson et al. (1958) obtained a poor antibody response in Icelandic children who, when vaccinated intradermally, were devoid of antibody.

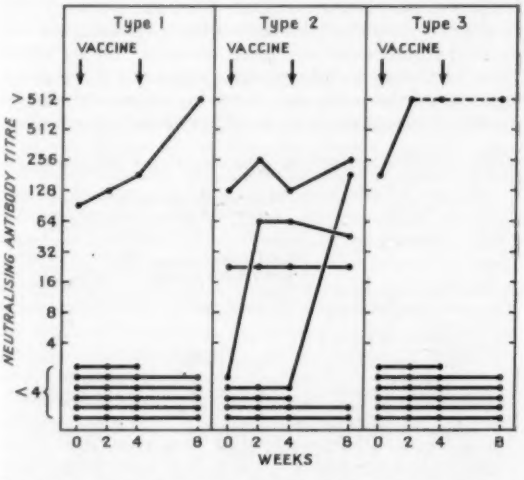

Fig. 3—The antibody response 4 weeks after two oral doses of vaccine.

Our results show that in most cases a booster response occurs in children already possessing naturally acquired antibody.

In assessing the results of vaccination it is important to know the antigenicity of the vaccine used. The British vaccine was tested by the manufacturer and the Medical Research Council before it was released. Dr. W. Wood informed us that, in the batches of vaccine used, the type-2 component was more antigenic than either the type-1 or type-3 component when tested in rhesus monkeys. This may account for more children showing a type-2 antibody response as seen in table III and table v. Salk (1955), however, has shown that the type-2 antibody response is enhanced by the presence of type-1 antibody and to a lesser degree by the presence of type-3 antibody. Of those children vaccinated intradermally who were devoid of type-2 antibody, 27 had type-1 antibody and 8 had type-3 antibody. The heightened type-2 antibody response may therefore be related to the presence of type-1 antibody. Salk (1957) has further shown that the proportion of people who respond to a vaccine, and the degree of response, is related to the mass of antigen administered. He demonstrated that the booster response to an intramuscular dose of 1 ml. was lower in those who initially had been vaccinated with two intradermal doses each of 0·1 ml. at two weeks' interval than after two intramuscular doses of 1 ml. He concluded that the intradermal method does not increase the efficiency of the antibody response sufficiently to permit reduction in the quantity of vaccine without sacrificing the effect in people who require more than very small quantities to produce an antibody response. While a third intradermal dose of vaccine may increase the number of people who respond (von Magnus 1957) it seems unlikely that the number responding will ever be so large, or the antibody titres so high, as in those who received a greater mass of antigen intramuscularly. It therefore appears that, in the absence of a more potent vaccine, the intradermal method has little to commend it for primary vaccination.

The response to formalinised poliomyelitis vaccine by mouth was poor, but the type-2 component appeared to be most antigenic. Because poliomyelitis is primarily an alimentary infection, Sabin (1956), Koprowski et al. (1956), Dane et al. (1957), and Dick et al. (1957) gave living attenuated poliomyelitis vaccines by mouth and antibody was subsequently produced. It is interesting that oral non-replicating polioviruses induced an antibody response in some children, and possibly the response might improve by using a larger dose or a more potent vaccine.

Summary

52 children under the age of five were given two intradermal doses of formalinised poliomyelitis vaccine and the antibody response was studied. This method was found to be unsatisfactory for primary vaccination in children initially devoid of antibody. Most children who possessed naturally acquired antibody showed a booster response.

Although an antibody response occurred in some

children after two oral doses of formalinised poliomyelitis vaccine, this method has no practical application at present.

We wish to thank the parents who gave consent for their children to take part in these trials; also Dr. B. R. Clarke, Dr. Sheila Balmer, and Dr. W. J. McLeod who gave valuable assistance. The work was supported by grants from the National Fund for Poliomyelitis Research, the Medical Research Council, and the Northern Ireland Hospitals Authority.

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INSULIN ANTAGONISM IN PLASMA OF DIABETIC PATIENTS AND NORMAL SUBJECTS

J. VALLANCE-OWEN
M.A., M.D. Cantab., M.R.C.P.
MEDICAL TUTOR AND SENIOR MEDICAL REGISTRAR, DEPARTMENT OF MEDICINE, POSTGRADUATE MEDICAL SCHOOL OF LONDON, W.12

ELIZABETH DENNES *
B.Sc. Birm., M.Sc. Lond., Ontario
RESEARCH ASSISTANT IN THE DEPARTMENT

P. N. CAMPBELL
Ph.D. Lond.
RESEARCH ASSISTANT, COURTAULD INSTITUTE OF BIOCHEMISTRY, MIDDLESEX HOSPITAL MEDICAL SCHOOL, LONDON, W.1

AMONG diabetic patients a group can be recognised in which, besides hyperglycæmia and glycosuria, ketosis and rapid loss of weight usually develop unless insulin is injected. In a study of the plasma-insulin activity in these patients using the rat diaphragm technique, it has been shown that, if the blood-sugar level is raised at the time of the test, no plasma-insulin activity is found. Moreover, when insulin is added in vitro to the plasma from these patients its activity is apparently inhibited (Vallance-Owen et al. 1955).

Plasma from normal subjects shows insulin activity and, when a known amount of insulin is added to the plasma in vitro, the activity of the added insulin is not diminished —i.e., there is no measurable antagonism (Vallance-Owen and Hurlock 1954). Nevertheless there is evidence that normal plasma contains an insulin antagonist, the action of which is masked. Thus if a normal cat is pancreatectomised, the plasma, which was previously inactive in the rat-diaphragm test, then antagonises added insulin (Vallance-Owen and Lukens 1957).

The experiments reported here were undertaken in an attempt to determine the chemical nature of the insulin antagonist, and to elucidate its mode of action.

Materials and Methods

Plasma

Venous blood was withdrawn into a heparinised syringe from non-fasting normal subjects and uncontrolled insulin-requiring diabetics who had received their last injection of soluble insulin at least 15 hours previously. The plasma was quickly separated by centrifugation.

* In receipt of a grant from the Medical Research Council.

Salt Fractionation of Plasma-proteins

Sodium sulphate (27% w/v) solution in phosphate buffer (pH 7·8, I=0·1) was added either to the fresh plasma or to reconstituted freeze-dried plasma to give various concentrations of the final solution between 15% and 22%. The precipitates were removed by centrifugation, and both fractions were dialysed against distilled water and freeze-dried.

Preparation of Albumin

Albumin was obtained from plasma by the trichloroacetic acid-ethanol procedure of Debro et al. (1957). In this procedure the 1% trichloroacetic acid (T.C.A.) in 96% aq. ethanol is added to 0·5 ml. of plasma to a final volume of 10 ml. The precipitate is removed by centrifugation, and the supernatant dialysed and freeze-dried. Later a modification of this procedure was adopted as follows:

An equal volume of 10% T.C.A. (w/v) was added to the plasma, the supernatant after centrifugation was discarded, and the precipitate washed with 5% T.C.A. The precipitate was then suspended in 1% T.C.A.: 96% aq. ethanol in a volume equivalent to three times the original volume of plasma. After centrifugation the extract was dialysed and freeze-dried.

Characterisation of the Plasma-protein Fractions

The fractions were subjected to paper electrophoresis in 'Veronal' buffer according to the method of Flynn and de Mayo (1951).

Measurement of Insulin Antagonism

Insulin antagonism was determined by the rat diaphragm assay procedure previously described (Vallance-Owen and Hurlock 1954, Vallance-Owen et al. 1955).

The freeze-dried fractions obtained were dissolved in buffer solution (Gey and Gey 1936) containing glucose (300 mg. per 100 ml.). Unless otherwise stated, the salt fractionated plasma proteins were dissolved at approximately the same concentration as they occurred in the original plasma.

Insulin was added to the buffer alone and to the buffer with the dissolved fraction to make a final concentration of 1000 micro-units per ml.

In any one experiment the glucose uptake of the diaphragm was determined in: (*a*) buffer alone (basal uptake); (*b*) buffer plus added insulin (standard); (*c*) buffer with dissolved fraction plus added insulin. The uptake was ordinarily measured three times in each solution, diaphragms from three different rats being used.

Results

Fractionation of Diabetic Plasma-proteins

As was found previously, full saturation of the diabetic plasma with sodium chloride precipitated the antagonistic activity of the plasma (Vallance-Owen and Lukens 1957). The active precipitate did not contain α_1-globulin but did contain a substantial amount of albumin. Owing to the poor fractionation of the plasma-proteins by this method, sodium sulphate was employed in subsequent experiments. The activity of the fractions obtained by sodium-

TABLE I—INSULIN ANTAGONISM OF FRACTIONS FROM DIABETIC PLASMA

Fraction	Mean glucose uptake above basal level ± standard error of the mean (mg. per 100 ml. per 10 mg. diaphragm)	
	Buffer + 1000 micro-units per ml. insulin	Fraction in buffer + 1000 micro-units per ml. insulin
Precipitate from 18% sodium sulphate	12·70 ± 0·91 (4)	13·17 ± 1·54 (4)
Supernatant from 18% sodium sulphate:		
Precipitate from 22% sodium sulphate	12·68 ± 0·64 (6)	3·02 ± 1·57 (6)
Supernatant from 22% sodium sulphate	11·43 ± 1·02 (9)	2·30 ± 1·14 (9)
Albumin:		
3·5–5·5%	12·22 ± 1·08 (4)	−0·37 ± 0·23 (4)
1·25%	12·32 ± 1·05 (4)	3·55 ± 0·67 (4)

Number of observations in parentheses.

sulphate fractionation of diabetic plasma is shown in table I. This shows that the precipitate obtained by saturation with 18% sodium sulphate was devoid of antagonistic activity, whereas the supernatant had such activity.

Paper electrophoresis showed that the sodium-sulphate fractionation effected a complete separation of the γ-globulin and albumin fractions—i.e., all the γ-globulin was in the precipitate and all the albumin in the supernatant. The other globulin components of the plasma were present in both fractions. It was concluded that the antagonistic activity was not associated with the γ-globulin fraction.

Attempts to fractionate the antagonistic activity of the supernatant from 18% sodium sulphate by higher concentrations of sodium sulphate were not successful (table I). These results were consistent with the idea that the activity was associated with the albumin in the diabetic plasma. Albumin was, therefore, prepared from diabetic plasma by the T.C.A.-ethanol method of Debro et al. (1957). As will be seen from table I, this albumin antagonised the effect of added insulin. The inhibition of the added insulin was complete when the concentration

TABLE II—INSULIN ANTAGONISM OF FRACTIONS FROM NORMAL PLASMA

Fraction	Mean glucose uptake above basal level ± standard error of the mean (mg. per 100 ml. per 10 mg. diaphragm)	
	Buffer + 1000 micro-units per ml. insulin	Fraction in buffer + 1000 micro-units per ml. insulin
Albumin (T.C.A.-ethanol) 3·5–5·5%	11·43 ± 0·62 (6)	0·50 ± 0·48 (6)
2·5%	12·63 ± 1·04 (3)	6·60 ± 1·01 (3)
1·25%	11·32 ± 0·74 (4)	11·17 ± 0·89 (4)
Albumin (ether fractionation) 5%	12·50 ± 1·40 (2)	2·75 ± 0·45 (2)
Albumin (Cohn Fraction V) 3·5%	12·40 (1)	2·40 (1)
Precipitate from 18% sodium sulphate	11·11 ± 0·34 (4)	15·61 ± 0·70 (4)
Supernatant from 18% sodium sulphate	12·42 ± 0·65 (4)	12·15 ± 0·22 (4)

Number of observations in parentheses.

of albumin in the buffer was between 3·5% and 5·5% which includes the physiological range. When the concentration was reduced to 1·25% there was still distinct antagonism of the added insulin. Paper electrophoresis of these albumin fractions failed to reveal any other plasma-protein.

Fractionation of Proteins from Normal Plasma

The demonstration of the presence of an insulin antagonist in the albumin from diabetic plasma prompted us to test the activity of a similar protein fraction from normal plasma. As will be seen in table II, this normal albumin in physiological concentration also had antagonistic activity. However, unlike albumin from diabetic plasma, a concentration of 1·25% failed to show any such antagonism. The possibility that this activity of normal plasma-albumin is due to a change in the albumin, associated with the T.C.A.-ethanol method of preparation, was tested by examining the activity of two samples of ether-fractionated albumin. As is shown in table II, these also inhibited the action of insulin. One sample of ethanol-fractionated plasma-albumin (Cohn fraction V) had similar activity. The possibility that the antagonistic activity was associated with a substance incapable of precipitation with T.C.A.—e.g., a polysaccharide—was excluded by changing the method of preparation of the albumin. Thus, when the plasma-proteins were precipitated with 5% T.C.A. and the albumin was extracted from the washed precipitate with ethanol, this albumin was fully active.

TABLE III—EFFECT OF THE SUPERNATANT FROM 18% SODIUM-SULPHATE-FRACTIONATED NORMAL PLASMA ON ALBUMIN FROM DIABETIC PLASMA

Fraction	Mean glucose uptake above basal level ± standard error of the mean (mg. per 100 ml. per 10 mg. diaphragm)	
	Buffer + 1000 micro-units per ml. insulin	Fraction in buffer + 1000 micro-units per ml. insulin
Supernatant from 18% sodium sulphate (7%) + 1·25% diabetic albumin	12·38 ± 0·70 (4)	3·20 ± 0·69 (4)

Number of observations in parentheses.

Since the albumin from normal plasma inhibited the action of insulin and yet the whole normal plasma did not exhibit any such antagonism, it was of interest to test the activity of fractions obtained from normal plasma by treatment with sodium sulphate. It will be seen from table II that, in contrast with the results with diabetic plasma, the precipitate obtained with 18% sodium sulphate stimulated the activity of insulin, and this supernatant was devoid of antagonistic activity. Since the amount of albumin in the supernatant would suffice to inhibit completely 1000 micro-units per ml. of insulin, it appears that normal plasma contains a substance which counteracts the antagonistic activity of the albumin. This substance could be insulin itself.

Effect of Fractions from Normal Plasma on Diabetic Plasma

The failure of the 18% sodium sulphate supernatant from normal plasma to antagonise the activity of added insulin suggested that this fraction might be capable of counteracting the effect obtained with diabetic albumin. That this was not so will be seen from table III. This suggests that the amount of substance with insulin-like activity in this normal plasma fraction is just sufficient to counteract the effect of the albumin present.

Nature of Insulin Antagonism by Diabetic Albumin

It seems unlikely that the ability of diabetic albumin to counteract the action of insulin on the rat diaphragm is due to a non-specific action on the metabolism of the tissue, for the following reasons: (1) the albumin in these physiological concentrations merely reduced the glucose uptake of the diaphragm to that achieved by the tissue in the absence of added insulin; (2) the addition of large amounts of insulin (i.e., 10,000 micro-units per ml.) partially counteracted the antagonism of the albumin. The results of the experiments illustrating this point are shown in table IV.

Discussion

These observations suggest that the previously described antagonism to insulin found in the plasma of insulin-

TABLE IV—EFFECT OF THE ADDITION OF 10,000 MICRO-UNITS PER ML. INSULIN TO ALBUMIN FROM NORMAL SUBJECTS

Fraction	Mean glucose uptake above basal level ± standard error of the mean (mg. per 100 ml. per 10 mg. diaphragm)	
	Buffer + 1000 micro-units per ml. insulin	Fraction in buffer + 10,000 micro-units per ml. insulin
Normal albumin (4%)*	12·33 ± 0·93 (4)	5·93 ± 0·67 (4)

Number of observations in parentheses.

* As will be seen from table II, albumin at this concentration completely antagonises the effect of insulin at 1000 micro-units per ml.

requiring diabetics resides in the albumin fraction. There is apparently similar antagonism in the plasma-albumin from normal subjects. However, the albumin fraction from normal subjects is less active in this respect. Bornstein and Park (1953) and Hendley et al. (1957) studied the plasma of alloxan-diabetic rats. They found that there was antagonistic activity in a lipoprotein fraction. Owing to the method of preparation of the albumin used in the present experiments it seems most unlikely that the antagonistic activity is associated with a lipoprotein. Moreover, the electrophoretic homogeneity of the T.C.A.-ethanol albumin preparations excludes the possibility that the activity is due to α_1-globulin. The homogeneity of such albumin preparations has been repeatedly studied (e.g., Schwert 1957). Thus the activity described here would seem to be different from that found by Field et al. (1957) in the α_1-globulin fraction of the plasma-proteins of severely ketotic diabetic patients.

Taylor (1958) has studied the distribution of insulin in fractions of human serum proteins. He finds that the maximal activity is in the region of the α_1-globulin when such proteins are subjected to zone electrophoresis, although insulin-like activity is also associated with the β- and γ-globulins. These results agree with ours, and explain why the precipitate obtained with 18% sodium sulphate, which contains all the γ-globulin, some of the β-globulin, but no albumin, stimulates the activity of insulin when isolated from normal plasma, but is without activity when isolated from diabetic plasma. The inactivity of the 18% sodium sulphate supernatant from normal plasma is probably due to the insulin associated with the α_1-globulin counteracting the effect of the albumin. Taylor also reports that the albumin fractions from human serum were inactive with the rat diaphragm test, although radioactivity studies showed that insulin is bound to the albumin even when isolated by the T.C.A.-ethanol method. These results are explicable on the basis that the activity of the insulin bound to the albumin is counteracted by the antagonistic activity of the albumin. On this basis it is also possible to explain the difference in activity between the diabetic albumin and the normal albumin; for the normal albumin will have some insulin bound to it, whereas the diabetic albumin will be relatively free of insulin.

The question as to whether the antagonistic activity is associated with the albumin per se or whether it is due to some substance bound to it must remain open. So far it has not been possible to prepare albumin which is devoid of antagonistic activity, but further work is in hand to elucidate this point.

In conclusion it would appear that human plasma-albumin preparations are able to counteract the action of insulin in stimulating the uptake of glucose by the rat diaphragm. The difference in antagonistic activity between the fractions from normal and diabetic subjects seems to be due to the presence or absence of insulin or an insulin-like substance. We suggest that, whatever the site and mode of action of insulin in carbohydrate metabolism, it has first to overcome the antagonistic activity of the plasma-albumin fraction.

Summary

Insulin antagonism has been found to reside in the albumin fraction of plasma from uncontrolled insulin-requiring diabetic patients and from normal subjects.

The antagonistic activity of the albumin in whole normal plasma is counteracted by some other substance —possibly insulin.

At present it is not known whether the antagonism is due to albumin itself or to a substance tightly bound to it.

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ARE IMMEDIATE HISTOLOGICAL EXAMINATIONS OF LUMPS IN THE BREAST USEFUL?

A. T. SANDISON
B.Sc., M.D. St. And.
LECTURER, UNIVERSITY DEPARTMENT OF PATHOLOGY, WESTERN INFIRMARY, GLASGOW

IT has been noticed in this hospital that the number of requests for immediate examination of lumps in the female breast has been slowly increasing. Since these examinations are rather time-consuming for the pathologist and especially for the laboratory technician, a small pilot survey of one hundred consecutive cases was undertaken to assess their value as a routine method.

A questionnaire was drawn up and completed as far as possible by the pathologist and the surgeon concerned in each instance. The information requested included, as well as the patient's name, age, ward, &c., the surgeon's diagnosis (with alternatives) before operation and after examination of the operative specimen, and the pathologist's diagnosis on naked-eye examination, on freehand section by Terry's method (Terry 1927, Lendrum 1951), and on examination of frozen sections stained with hæmalum and eosin. In all the cases the final diagnosis was established by conventional paraffin embedding and section.

Methods and Material

Technique

Malignancy can often be determined by inspection or, more often, by careful palpation. The examination of immediate sections either prepared by Terry's method or frozen is facilitated by using a very bright source of light. The most valuable microscope objective is the scanning (40 mm. x 4; supplied by Watson's of London); this gives an excellent topographical view of the mammary architecture which is so important in this form of microscopy. This can be ideally combined with a X6

TABLE I—AGE-DISTRIBUTION

Age (yr.)	Present series (100 cases)	Large series (1010 cases)
20–29	2%	7%
30–39	14%	15%
40–49	52%	32%
50–59	19%	18%
60–69	7%	14%
70–79	5%	7%
80–89	1%	1%

TABLE II—DIAGNOSES ON PARAFFIN SECTION

—	Present series (100 cases)	Large series (1010 cases)
Carcinoma	50%	50%
Fibrocystic	26%	15%
Hyperplastic cystic (epitheliosis)	10%	10%
Fibroadenoma	5%	10%
Fat-necrosis	4%	1%
Involutional change	2%	—
Papilloma	1%	4%
Inflammation	1%	3%
Leiomyoma of skin	1%	—

long-focus wide-angle eyepiece (or eyepieces if a binocular microscope is used)—e.g., the 'Complec' (Watson) or the 'Telaugic' (Swift).

Age of Patients

The age-distribution of the patients is shown in table I. For comparison the ages in a larger consecutive series of breast operations in the Western Infirmary, Glasgow, are also given (Sandison 1958). It will be seen that immediate examination was requested in women of widely varied ages. The highest incidence of request falls in the fifth decade of life.

Type of Case

Table II shows the final diagnosis, and again the larger series is given for comparison. In both series carcinoma accounted for 50% of cases. Immediate examination was requested for a higher proportion of lumps which proved to be fibrocystic disease and for a smaller proportion proving to be fibroadenoma, papilloma, or inflammation.

Results

Diagnostic Errors of Surgeon

These are shown in table III. The surgeon was wrong in 25% of preoperative diagnoses, and a wrong diagnosis of malignancy (16%) was commoner than failure to diagnose malignancy (9%). At operation no opinion was given in 3%, but the diagnostic error was much reduced (9%), and failure to diagnose malignancy (6%) was commoner than wrong diagnosis of malignancy (3%). In 3 of the failures to diagnose malignancy the pathologist's diagnosis was also wrong on naked-eye examination.

Diagnostic Errors of Pathologist

These are shown in table IV.

Naked-eye examination.—The pathologist improved slightly on the surgeon's rate of diagnostic error—6% against 9%. Most of these errors were failure to diagnose malignancy (5%), and in only 1% was a wrong diagnosis of malignancy made.

TABLE III—DIAGNOSTIC ERRORS OF SURGEON

—	Preoperative	At operation
Number of cases	100	100
No opinion	—	3
Number correct	75	88
Number of errors	25	9
Failure to diagnose malignancy	9	6*
Wrong diagnosis of malignancy	16	3

* In 3 of these the pathologist also was in error on morbid anatomy.

TABLE IV—DIAGNOSTIC ERRORS OF PATHOLOGIST

—	Morbid anatomy	Terry section	Frozen section
Number of cases	100	87	89
No opinion	2	1	—
Number correct	92	97	97
Number of errors	6	2	3
Failure to diagnose malignancy	5	1	1
Wrong diagnosis of malignancy	1	1	2

Freehand section stained by Terry's method.—In this technique a freehand section cut with a razor or a safety-razor blade is stained by polychrome methylene-blue. In 12% of the cases this technique was not used, because it was thought unnecessary owing to the obvious diagnosis on naked-eye examination. It should be remembered, however, that malignant change may be present in association with large simple cysts. In 1 other case no section was made, because of technical difficulty, the specimen being a mucoid carcinoma. Of the 87 cases examined, in 1 case no opinion was given, and in 2 the diagnosis was wrong: in one case a puerperal carcinoma was not diagnosed, because of the predominantly inflammatory picture; and in the other case a large intracanalicular fibroadenoma was misdiagnosed as sarcoma.

Frozen section stained with haemalum and eosin.—In 10 cases no frozen section was prepared, because it was thought unnecessary owing to the obvious diagnosis on naked-eye examination. In 4 of these cases, all cysts, neither Terry examination nor frozen section was considered necessary. In 1 other case no section was made, because of the smallness of the specimen and the necessity of conserving tissue for formal paraffin section. In the 89 cases examined 3 diagnostic errors were made: 2 of these were identical with the errors made on freehand section stained by Terry's method; in the 3rd, epitheliosis with lipophagic reaction was misdiagnosed as the intraduct carcinoma of Paget's disease.

Credits and Debits

Unnecessary mastectomy was avoided in 8 cases: in 4 the surgeon had said he would have done a radical mastectomy if immediate examination had not been available, and in the 4 others the intention had been to do a simple mastectomy.

In 2 cases unnecessary simple mastectomies were done on the advice of the pathologist: in one case for intracanalicular fibroadenoma wrongly thought to be sarcoma, and in the other for epitheliosis misdiagnosed as intraduct carcinoma.

In the case of puerperal carcinoma it had already been decided that no further operation was contemplated, and that radiotherapy should be used if the paraffin section showed carcinoma.

Time Factors

In 80 cases the time of interruption of the operation averaged 7 minutes. On the other hand, the average time spent by the pathologist in 42 cases was 40 minutes. In most cases this was accounted for by time spent in waiting for the specimen to be obtained. In the other cases the times were not recorded.

Conclusions

In 100 consecutive cases of lump in the breast for which immediate histological examination was requested some observations were made. Surgical diagnosis of the presence or absence of malignancy was correct in 75% of cases before operation and in 88% at operation. Before operation the tendency was to overdiagnose malignancy and at operation to fail to diagnose malignancy. The pathologist made the correct diagnosis in 92% of cases on naked-eye examination. In 3% of cases the diagnosis reached on Terry section and/or frozen section was incorrect. 8 unnecessary mastectomies (4 of which would have been radical) were avoided, but 2 unnecessary simple mastectomies were done despite immediate histological examination. It should be emphasised that these examinations

were made by ten pathologists as part of their routine duties. The results are not claimed to approach those of pathologists who have made a special study of this method.

The technique of immediate section does not greatly interrupt the surgeon but is time-consuming (in terms of waiting) for pathologist and technician. This is the major economic argument against the method. The materials used cost only a few shillings, the bulk of this being the cost of the carbon dioxide used.

On balance it seems that immediate histological examination of lumps in the breast is worth while.

Summary

100 consecutive cases of immediate histological examination of lumps in the female breast were studied.

There is a place for this technique in handling some cases of lump in the breast.

I am grateful to my colleagues in the pathology department of the Western Infirmary, Glasgow, for their patience in filling in the relevant questionnaire, and to the surgeons of the Western Infirmary for assisting in this investigation. Dr. Bernard Lennox compiled the original questionnaire.

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THYROTOXICOSIS WITH GLYCOSURIA AND ADRENOCORTICAL HYPERACTIVITY

F. D. ROSENTHAL
M.D. Lond., M.R.C.P.
FORMERLY SENIOR MEDICAL REGISTRAR *

F. LEES
M.B. Sheff., M.R.C.P., D.C.H.
FORMERLY MEDICAL REGISTRAR †

ROYAL INFIRMARY, SHEFFIELD

WE have recently seen three men with thyrotoxicosis in whom the excretion of urinary 17-ketogenic steroids was increased. Our attention was drawn to the first of these cases because the patient had glycosuria and gynæcomastia. The second patient had glycosuria; and when the third presented with glycosuria and gynæcomastia we felt confident that his 17-ketogenic-steroid output would be increased, and this proved to be the case.

The exact relation of thyroid to adrenal cortical function has still not been fully determined.

In thyrotoxicosis the urinary excretion of 17-ketosteroids has generally been found to be normal or reduced (Engstrom and Mason 1944, Escamilla 1949). Indirect tests of adrenocortical function, such as the eosinophil response to corticotrophin and the insulin-sensitivity test, have been reported to show no abnormality (Hill et al. 1950, Hernberg and Lamberg 1955). Levin and Daughaday (1955) found the urinary excretion of 17-hydroxycorticoids to be normal, but they showed that hydrocortisone disappeared from the plasma more rapidly than in healthy subjects.

A raised output of urinary 17-ketogenic steroids in thyrotoxicosis appears to be uncommon. In an unselected group of eight men and twenty-four women with thyrotoxicosis Levell et al. (1957) found the output of urinary 17-ketogenic steroids to be raised in one man and two women (M. J. Levell, personal communication). In a highly selected group of two men and five women with thyrotoxicosis and diabetes these workers found the urinary 17-ketogenic steroid excretion to be raised in one man and all five women. Two of the women were reported in detail by Hubble (1955); the man is case 1 of the present group of cases.

The cause of the increased excretion of 17-ketogenic steroids is at present uncertain, and we have carried out studies in our three cases to try and determine its mechanism. Our work throws no light on the problem why adrenocortical activity should be increased in some cases of thyrotoxicosis and not in others. The findings of M. J. Levell (personal communication) do not suggest that adrenocortical changes in thyrotoxicosis are more common in one sex than the other, and we feel that the mode of presentation with gynæcomastia in two of our cases has produced a sex bias in this study.

Case-records

Case 1.—A miner, aged 41, was seen as an outpatient on April 30, 1956. After a dental extraction 12 months previously he had lost 24 lb. (10·5 kg.) in weight. For 8 months he had felt tired and had little energy. He was thirsty, and as a result of an increased fluid intake passed large quantities of urine. He became intolerant of heat and sweated easily. For 6 months he had been nervous and tremulous. He noticed palpitations, particularly in bed at night, and was short of breath on exercise. For 2 months his breasts had been sore. His sister suffered from diabetes mellitus.

On examination he was thin, nervous, and sweating; bodyweight 129 lb. (58·6 kg.). Moderate exophthalmos was present. The thyroid was moderately enlarged, lobulated, and firm. The hands were warm and moist; there was a fine tremor of the outstretched hands. Pulse regular, rate 120 per min.; blood-pressure 150/70 mm. Hg. The breasts were slightly enlarged, firm, and tender. The nipples were normal; milk could not be expressed. The urine gave an orange reaction with Benedict's reagent.

Investigations.—A radioactive-iodine-tracer test confirmed the diagnosis of thyrotoxicosis; the 4-hour thyroid uptake of iodine was 69·4% of the dose given, and the 48-hour protein-bound iodine 4·36% of the dose given per litre of plasma. The 24-hour urinary excretion of 17-ketosteroids was 13·5 mg. and of 17-ketogenic steroids 28·8 mg. The fasting blood-sugar was 150 mg. per 100 ml.; 1 hour after the ingestion of 50 g. of glucose the blood-sugar was 265 mg. per 100 ml., and after 2 hours it was 125 mg. per 100 ml. Radiographs of the skull and chest were normal. The Wassermann reaction was negative. The erythrocyte-sedimentation rate (E.S.R.) was 28 mm. in the 1st hour (Wintrobe); hæmoglobin 14·0 g. per 100 ml.

Treatment was with carbimazole 10 mg. three times daily by mouth.

Admission.—He was admitted on Aug. 7, 1956, for further studies. He was found to be myxœdematous with the typical facial appearance and voice change of this condition. The basal metabolic rate was −26% (average of four readings) and the serum-cholesterol 455 mg. per 100 ml. The 24-hour urinary 17-ketosteroid excretion was 9·1 mg., and that of 17-ketogenic steroids 11·9 mg. During the administration of prednisolone 20 mg. 6-hourly for 3 days the 24-hour urinary excretion of 17-ketosteroids dropped to 3·9 mg., and the 17-ketogenic-steroid excretion rose to 17·2–25·3 mg. The administration of corticotrophin 100 units by intravenous drip daily for 2 days raised the 24-hour urinary excretion of 17-ketosteroids to 34·1 mg. and of 17-ketogenic steroids to 87·8 mg. The fasting blood-sugar was 105 mg. per 100 ml.; following the ingestion of 50 mg. of glucose the blood-sugar was 224 mg. per 100 ml. after 1 hour, and 156 mg. per 100 ml. after 2 hours. The patient was discharged on Aug. 19, 1956.

Second admission.—He was readmitted on Oct. 12, 1956, having had no antithyroid treatment in the meantime. He was thyrotoxic; the basal metabolic rate was +40% (average of four readings) and the serum-cholesterol 230 mg. per 100 ml.

* Present address: Department of Neurology, Queen Elizabeth Hospital, Birmingham, 15.
† Present address: Department of Neurology, Royal Infirmary, Manchester, 13.

The 24-hour urinary 17-ketosteroid excretion was 14·8 mg., that of 17-ketogenic steroids 31·6 mg. Following the administration of prednisolone 20 mg. 6-hourly for 3 days the 24-hour urinary excretion of 17-ketosteroids was 11·5 mg. and of 17-ketogenic steroids 10·1 mg. The administration of corticotrophin 100 units by intravenous drip daily for 2 days increased the 24-hour urinary excretion of 17-ketosteroids to 14·7 mg. and of 17-ketogenic steroids to 45·8 mg. The fasting blood-sugar was 84 mg. per 100 ml.; following the ingestion of 50 g. of glucose the blood-sugar level was 216 mg. per 100 ml. after 1 hour, and 105 mg. per 100 ml. after 2 hours. A further glucose-tolerance curve showed the fasting blood-sugar to be 90 mg. per 100 ml.; following ingestion of 50 g. of glucose the blood-sugar was 264 mg. per 100 ml. after 1 hour, 156 mg. per 100 ml. after 2 hours, and 120 mg. per 100 ml. after $2^1/_1$ hours.

Progress.—The patient was discharged on Oct. 27, 1956, and the thyrotoxicosis has since been controlled by carbimazole 10 mg. three times daily. His gynæcomastia has disappeared.

Case 2.—A car deliverer, aged 55, was seen as an outpatient on Dec. 24, 1956. He had not been well for about 10 months, during which time he had lost 35 lb. (16 kg.) in weight. For 9 months he had sweated easily, had been trembly, disliked warm weather, and suffered palpitations with shortness of breath on exercise. For 3 months his eyes had been prominent and occasionally he saw double. He had become nervous and depressed.

On examination he was thin, nervous, and sweating; body-weight 142 lb. (64·5 kg.). Both eyes, especially the right, were prominent and both eyelids were œdematous. The thyroid was only just palpable; it was smooth and firm. The hands were warm and moist with a fine tremor. He had auricular fibrillation with heart-rate of 116 per min.; blood-pressure 140/70 mm. Hg. The urine gave a yellow reaction with Benedict's reagent.

Investigations.—A radioactive-iodine-tracer test confirmed the diagnosis of thyrotoxicosis; the 4-hour thyroid uptake of iodine was 67·5% of the dose given, and the 48-hour protein-bound iodine 1·23% of the dose given per litre of plasma. The 24-hour urinary excretion of 17-ketosteroids was 10·6 mg., of 17-ketogenic steroids was 24·8 mg., and of gonadotrophins 8 mouse units. The fasting blood-sugar was 110 mg. per 100 ml.; following the ingestion of 50 g. of glucose the blood-sugar level was 160 mg. per 100 ml. after 1 hour, and 79 mg. per 100 ml. after 2 hours. Radiographs of the skull and chest were normal. An electrocardiogram confirmed the presence of auricular fibrillation. The Wassermann reaction was negative. The E.S.R. was 11 mm. in the 1st hour (Wintrobe); the hæmoglobin was 13·2 g. per 100 ml.

Admission.—The patient was admitted on Jan. 15, 1957, for further studies. The basal metabolic rate was +28% (average of four readings) and the serum-cholesterol 245 mg. per 100 ml. The 24-hour urinary excretion of 17-ketosteroids was 8·7 mg., of 17 ketogenic steroids 36·5 mg., and of gonadotrophins 5 mouse units. During the administration of prednisolone 20 mg. 6-hourly for 3 days the 24-hour urinary excretion of 17-ketosteroids fell to 5·8 mg., and that of 17-ketogenic steroids varied between 23·2 and 42·5 mg. During the administration of corticotrophin gel 20 mg. 12-hourly intramuscularly for 2 days the urinary 24-hour excretion of 17-ketosteroids was 9·5 mg. and 13·3 mg., and that of 17-ketogenic steroids was 40·5 mg. and 47·7 mg. The fasting blood-sugar was 70 mg. per 100 ml.; following the ingestion of 50 g. of glucose the blood-sugar was 204 mg. per 100 ml. after 1 hour, and 108 mg. per 100 ml. after 2 hours.

Progress.—The patient was discharged on Feb. 5, 1957, and since then his thyrotoxicosis has been controlled by carbimazole. When he was seen as an outpatient on Nov. 18, 1957, his auricular fibrillation had ceased and his pulse-rate was 80 per min. He appeared euthyroid and the serum-cholesterol was 250 mg. per 100 ml. The 24-hour urinary excretion of 17-ketosteroids was 10·0 mg. and of 17-ketogenic steroids 15·4 mg. The fasting blood-sugar level was 100 mg. per 100 ml.; following the ingestion of 50 g. of glucose the blood-sugar was 150 mg. per 100 ml. after 1 hour, and 60 mg. per 100 ml. after $2^1/_2$ hours.

Case 3.—A telephone engineer, aged 48, was seen as an outpatient on Sept. 12, 1957. He had not felt well for about 9 months during which time he had lost about 14 lb. (6·5 kg.) in weight. He sweated a great deal and had become intolerant of warm weather. He felt nervous and trembly; on exercise he was short of breath and had palpitations. He had started to be thirsty, and as a result of the increased fluid intake passed large quantities of urine. For 2 months his breasts had been tender and painful, so that he had to give up wearing braces.

On examination he was nervous and sweating; body-weight 139 lb. (63 kg.) The eyes were prominent and the eyelids œdematous. The thyroid was impalpable. There was fine tremor of the outstretched hands. The pulse was regular, rate 108 per min.; blood-pressure 130/70 mm. Hg. The breasts were slightly enlarged, uniformly firm, and tender; the nipples were normal; milk could not be expressed. The urine gave a yellow reaction with Benedict's reagent.

Investigations.—A radioactive-iodine-tracer test confirmed the diagnosis of thyrotoxicosis; the 4-hour thyroid uptake of iodine was 79·8% of the dose given, and the 48-hour protein-bound iodine was 2·34% of the dose given per litre of plasma. The 24-hour urinary excretion of 17-ketosteroids was 15·4 mg. and 11·1 mg., of 17-ketogenic steroids 23·7 mg. and 27·2 mg., and of gonadotrophins 25 mouse units. The fasting blood-sugar was 83 mg. per 100 ml.; following the ingestion of 50 g. of glucose the blood-sugar was 160 mg. per 100 ml. after $^1/_2$ hour, 140 mg. per 100 ml. after 1 hour, and 75 mg. per 100 ml. after 2 hours. The serum-cholesterol was 140 mg. per 100 ml. Radiographs of the skull and chest were normal. The Wassermann reaction was negative. The E.S.R. was 15 mm. in the 1st hour (Wintrobe); the hæmoglobin was 14·2 g. per 100 ml.

Treatment and progress.—The patient was treated with carbimazole 10 mg. three times daily by mouth, and when seen as an outpatient on Jan. 9, 1958, he appeared euthyroid. The gynæcomastia had disappeared. The serum-cholesterol was 280 mg. per 100 ml. The 24-hour urinary excretion of 17-ketosteroids was 8·6 mg. and of 17-ketogenic steroids 8·2 mg.* The fasting blood-sugar was 73 mg. per 100 ml.; following the ingestion of 50 g. of glucose the blood-sugar was 120 mg. per 100 ml. after 1 hour, and 55 mg. per 100 ml. after 2 hours.

Discussion

Thyrotoxicosis with exophthalmos is generally regarded as pituitary in origin (Naffziger 1954). In our three cases in addition to a state of thyroid stimulation there was increased excretion of adrenocortical hormones—which suggested that adrenocortical stimulation was also present. In the study of his two cases of thyrotoxicosis with diabetes mellitus and adrenocortical hyperactivity, Hubble (1955) thought that panhyperpituitarism was the primary abnormality. One of the most striking features of our cases was that when a euthyroid or myxœdematous state was reached adrenocortical hyperactivity ceased. This suggested that the thyrotoxicosis itself was the cause of the adrenocortical overaction. Hubble (1955) in one of his cases also found that the adrenocortical hyperactivity decreased once the thyrotoxicosis was under control.

In thyrotoxicosis uncomplicated by diabetes the fasting blood-sugar is normal, but the renal threshold is commonly lowered and rapid absorption of glucose may raise the blood-sugar sufficiently to produce glycosuria (John 1932, Spence 1953). This appeared to be the cause of the glycosuria in the present case 3, and his oral glucose-tolerance curve became normal once the thyro-

toxicosis was controlled. It was probably also the cause of the glycosuria in case 2, but it was difficult to explain the first fasting blood-sugar of 110 mg. per 100 ml. and also the fasting blood-sugar of 100 mg. per 100 ml. once he was euthyroid. In patients who have recovered from thyrotoxicosis the incidence of diabetes is greater than in the general population (John 1932). This is unlikely to be of adrenocortical origin as steroid diabetes has been reported to be nearly always reversible once adrenocortical hyperactivity ceases (Frawley 1955). Houssay (1944) has shown that prolonged administration of thyroid extract to normal dogs has no permanent effect on glucose tolerance, but that in non-diabetic partially depancreatised dogs irreversible diabetes frequently results. Case 1 as well as case 1 of Hubble (1955) had a family history of diabetes, and the failure of their diabetes to improve once the thyrotoxicosis was controlled may have been due to their being potential diabetics before the onset of thyrotoxicosis.

Gynæcomastia in thyrotoxicosis was already known to von Basedow (1848) and more recently has been observed by Sterling (1932), Starr (1935), and Ballinger (1947). One of the cases of Starr (1935) had testicular atrophy, and the case of Ballinger (1947) had undescended testes; but their gynæcomastia only developed with the onset of thyrotoxicosis. The gynæcomastia in these two cases, as in the second case of Starr (1935), disappeared following thyroidectomy. Gynæcomastia appeared in the present cases 1 and 3 as the symptoms of thyrotoxicosis became prominent; it regressed when the patients became euthyroid on carbimazole. Gynæcomastia cannot be regarded as indicating hyperpituitarism and may occur in many endocrine and non-endocrine conditions (Menville 1933, Spence 1953). It can be of purely adrenal origin and has been observed after administration of adrenocortical extracts and deoxycortone (Edwards et al. 1938, Laurence 1943).

In our cases there were no features suggesting acromegaly, and estimation of the urinary gonadotrophins in cases 2 and 3 showed their excretion to be within normal limits. In our three cases and in the two cases reported by Hubble (1955) only the excretion of urinary 17-ketogenic steroids was increased and the urinary 17-ketosteroids were normal. These results suggested hypertrophy of the zona fasiculata, the main secretor organ of glucocorticoids, and a normal zona reticulata, which produces androgens (Landing 1955). Such findings were in agreement with those of Deane and Greep (1947), who in thyrotoxic dogs found the zona fasiculata hypertrophied and overactive, but the zona reticulata unaffected. The increased output of 17-ketogenic steroids in our patients was unaccompanied by the usual signs of glucocorticoid overproduction and moon-face, hypertension and polycythæmia were not seen. This combination of increased glucocorticoid excretion without the signs of Cushing's syndrome has been shown by Ingle (1952) to characterise the response to stress by the adrenal cortex. Such conditions have been observed after surgery and have occasionally been seen in cases of cancer (Hardy et al. 1953, Hardy 1953, Jepson et al. 1956).

The mechanism of the adrenocortical hyperactivity does not appear to us to be of primary pituitary or of primary adrenal origin, as control of the thyrotoxicosis resulted in normal adrenocortical function. This result was achieved by carbimazole, which has no direct action on the pituitary or adrenal. It seems clear that the thyroid overactivity acting through the pituitary or the adrenal cortex may have been the fundamental cause of the overactive adrenal cortex. This appeared to be the most important result of our investigations. It is strongly supported by the work of Deane and Greep (1947), who showed that the administration of thyroid extract to thyroidectomised dogs rendering them thyrotoxic produced hypertrophy and hyperactivity of the zona fasiculata and the zona glomerulosa. It seems to us most likely that the effect of the thyrotoxicosis is on the pituitary, being comparable with reactions to other systemic diseases which have been described as inducing an increased output of corticotrophin (Currie and Symington 1955).

Summary

Three cases of men with thyrotoxicosis, in whom a high urinary excretion of 17-ketogenic steroids indicated adrenocortical hyperactivity, are described.

All three patients had glycosuria, and two had gynæcomastia.

On treatment with carbimazole the patients became euthyroid or myxœdematous; adrenocortical hyperactivity ceased, and the gynæcomastia disappeared.

There were no signs of acromegaly or of Cushing's syndrome, and the urinary excretion of gonadotrophins was normal in the two cases where they were estimated.

Apparently the primary cause of the increased adrenocortical activity was the thyrotoxicosis, and the adrenocortical hyperactivity was not primarily pituitary or adrenal in origin.

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". . . On the humanitarian view all crime is pathological; it demands not retributive punishment but cure. This separates the criminal's treatment from the concepts of justice and desert; a 'just cure' is meaningless. On the old view public opinion might protest against a punishment (it protested against our old penal code) as excessive, more than the man 'deserved'; an ethical question on which anyone might have an opinion. But a remedial treatment can be judged only by the probability of its success; a technical question on which only experts can speak. Thus the criminal ceases to be a person, a subject of rights and duties, and becomes merely an object on which society can work. And this is, in principle, how Hitler treated the Jews. They were objects; killed not for ill desert but because, on his theories, they were a disease in society. If society can mend, remake, and unmake men at its pleasure, its pleasure may, of course, be humane or homicidal. The difference is important. But either way, rulers have become owners."—Prof. C. S. Lewis, *Observer*, July 20, 1958.

VAGOTOMY IN HYPERTROPHIC PULMONARY OSTEOARTHROPATHY ASSOCIATED WITH BRONCHIAL CARCINOMA

R. L. HUCKSTEP
M.A., M.D. Cantab., F.R.C.S.E.
LATE THORACIC SURGICAL HOUSE-SURGEON

P. E. BODKIN
M.B. Cantab., F.F.R.
REGISTRAR, MEYERSTEIN INSTITUTE OF RADIOTHERAPY

MIDDLESEX HOSPITAL, LONDON, W.1

SINCE Hippocrates first described clubbing of the fingers and toes in the 5th century B.C. there have been numerous descriptions of the condition, including an important publication by Mendlowitz (1942). Some of the underlying pathological causes include pulmonary and cardiac conditions, ulcerative colitis, steatorrhœa, cirrhosis of the liver, roundworm infestation, and, rarely, thyroidectomy (Mendlowitz 1942).

In some cases finger clubbing may be associated with incapacitating hypertrophic osteoarthropathy.

The most common cause of severe osteoarthropathy is bronchial carcinoma. The proportion of bronchial carcinoma reported as showing painful osteoarthropathy varies from 1–2% (Semple and McCluskie 1955) and 5–10% (Flavell 1956) up to 50% (Alvarez 1948). The incidence is probably well under 5%. It is peripheral carcinoma rather than the central tumour which is more commonly associated with osteoarthropathy. The peripheral type is a relatively uncommon form of lung carcinoma, and is often a localised lesion involving neither pleura nor hilum. It is usually surprisingly small in view of the severity of the symptoms in the limbs.

Often a quite astonishing improvement takes place after pneumonectomy or even after local removal of the tumour. There is often complete loss of pain within a few hours, and the effusions in the joints may improve after a few days. The clubbing of the fingers and toes sometimes progressively improves, the nails returning to normal as the nail grows out (Flavell 1956).

The satisfactory results of resection in man are also seen in the dog (Lumb and Carlson 1956). Simple operations have had an equally satisfactory effect on pulmonary osteoarthropathy—e.g., ligation of the pulmonary artery on the side of the lesion (Wyburn-Mason 1948) and denervation of the lung hilum in inoperable carcinoma (Brea 1948, Hansen 1954). In these operations division of the nerve-supply was apparently the deciding factor in relieving the joint symptoms, rather than any direct interference with the tumour. Following these observations and his own previous results of attempted removal, Flavell (1956) denervated the hilum in two cases of inoperable carcinoma with equally satisfactory results. The effect was then tried, in three cases, of simple division of the vagus immediately above the hilum without disturbing the hilar structures; the pulmonary osteoarthropathy in all three cases subsided immediately.

Fig. 1—Case 1: œdema of hands and clubbing of fingers.

In view of the remarkable palliation observed by Flavell, vagotomy was done in two advanced cases of unresectable pulmonary carcinoma with severe osteoarthropathy. In one case the osteoarthropathy was so incapacitating, with both hands and feet extremely painful and swollen, that the patient was completely crippled.

Case-reports

Case 1.—A man, aged 64, was admitted to hospital in May, 1956, with advanced pulmonary osteoarthropathy. Severe pain limited the movements of his hands, elbows, feet, and knees. He was bedridden. The symptoms had started in March, 1956, a week after an attack of pneumonia. He had been a coalminer many years previously and had been a heavy smoker.

Fig. 2—Case 1: tomograph showing rounded mass in upper lobe of left lung.

On examination his general condition was poor. His hands were swollen with œdema and showed severe clubbing (fig. 1). Pain was particularly severe in his right hand, wrist and, elbow. He had massive œdema of his ankles and feet with extreme tenderness. Air entry was diminished over his left upper lobe, and numerous rhonchi were heard over his left lung. He was dyspnœic on the slightest exertion and had marked bilateral gynæcomastia. There were no other relevant findings.

Radiography of his chest showed a peripheral rounded opacity in the upper lobe of the left lung. Tomography showed that this opacity was homogeneous and had rather ill-defined margins, suggesting a bronchial carcinoma (fig. 2).

Bronchoscopy showed no abnormality. Severe bronchitis contra-indicated resection.

Treatment.—Three days after admission, deep X-ray therapy was begun and a tumour dose of 3485r was given over thirty days. In spite of this there was no improvement in the severe pain of the osteoarthropathy, the dyspnœa was not alleviated, and the patient remained completely bedridden. Although his very poor condition made him a grave operative risk, it was thought justifiable to try the effect of vagotomy, without attempting to remove the tumour.

Operation.—A left lateral thoracotomy was done in June, 1956, by Mr. J. R. Belcher. The vagus nerve was identified and divided beneath the arch of the aorta immediately below the point where the recurrent laryngeal nerve was given off. No other structures were disturbed.

Postoperative course.—Within twenty-four hours all the

pains in the bones and joints were relieved, the swelling and œdema of the hands and feet were regressing, and the movements of the hands and fingers had much improved. In three days the œdema had completely disappeared, the dyspnœa was considerably improved, and the patient got up. At the end of ten days he was walking round the ward pain-free.

Discharge and follow-up.—He was discharged from hospital on the thirteenth postoperative day. On the twenty-fifth postoperative day he walked into the outpatients clinic without any pain, œdema, or gynæcomastia. He was last seen nine months later, when he complained of considerable loss of weight and vomiting. His general condition was deteriorating, and his liver was grossly enlarged, but he still had no pain or œdema, although the clubbing was still present. He was not dyspnœic and had no gynæcomastia.

Case 2.—A man, aged 57, was admitted in August, 1956, complaining of feeling unwell and of having lost weight since an attack of "influenza" in February. Since May, 1956, he had noticed clubbing of his fingers and toes and had increasing painful swelling of his ankles and knees. Mild dyspnœa had been present for the same period. He had smoked heavily for forty years.

On examination he had marked clubbing of his fingers and toes and swelling of his ankles and knees. Movement of these joints was painful and limited.

Radiography of his chest showed a large rounded mass in the right mid-zone, extending outwards to the chest wall in the axilla (fig. 3).

Bronchoscopy showed a submucous infiltration of the lateral wall of the right main bronchus, and biopsy of this area disclosed a poorly differentiated carcinoma.

Operation.—A right thoracotomy was done in August, 1956 by Mr. J. W. Jackson. A growth was found in the right upper lobe, extending across the oblique fissure but not adherent to the parietal pleura. Large lymph-nodes involved by carcinoma in the hilum made the growth inoperable. The vagus nerve was therefore identified above the hilum and divided.

Postoperatively the relief of pain was immediate and the œdema disappeared within forty-eight hours. On the thirteenth postoperative day a course of deep X-ray therapy to the primary tumour and to bilateral supraclavicular glands which had appeared since the operation, was begun. A tumour dose of 2834r was given over three weeks. The patient was discharged from hospital on Sept. 24, 1956.

Follow-up.—In January, 1957, he had a second palliative course of deep X-ray therapy to secondary deposits in his pelvic bones, ribs, and cervical lymph-nodes. Despite progression of his metastases he had no further symptoms from his pulmonary osteoarthropathy. There was no change in the degree of clubbing. His general condition continued to deteriorate, and he died in March, 1957.

Fig. 3—Case 2: radiograph showing rounded mass in right mid-zone of chest.

Discussion

Both patients had severe pulmonary osteoarthropathy, of which pain was the prominent symptom. This pain completely overshadowed the pulmonary symptoms of carcinoma.

The rapid and complete relief of pain in the joints, followed by resolution of the swelling and œdema, confirm the finding of Flavell (1956). An unusual feature was the bilateral gynæcomastia in case 1, which regressed after vagotomy. The association of gynæcomastia with carcinoma of the bronchus has been noted previously; Stephens (1928) reported an incidence of 7%, and Semple and McCluskie (1955) of 8·3%. No case has hitherto been reported which had been successfully treated by vagotomy.

Although the causation of osteoarthropathy is unknown, the nervous theory of Cudkowicz and Armstrong (1953) appears to be the soundest. They postulate a pulmonary autonomic systemic vascular reflex by which ischæmia in parts of the lung distal to the tumour reflexly cause systemic arteriovenous anastomoses to open up in the limbs.

In the present two cases the following points support the theory that hypertrophic pulmonary osteoarthropathy is primarily due to a nervous and not a chemical mechanism:

(1) If osteoarthropathy were caused by a chemical substance liberated by the tumour, one would expect that the most severe manifestations would be associated with tumours with extensive secondary deposits. Local removal of a small tumour, however, may give remarkable and usually permanent relief from osteoarthropathy. It is uncommon for pain and swelling to occur after resection, even though extensive metastases develop later.

(2) The associated gynæcomastia could be explained by the pulmonary autonomic systemic vascular reflex theory, arteriovenous anastomoses opening up in the breast as in the limbs.

(3) Many lesions, totally different in ætiology and pathology, produce the manifestations of hypertrophic pulmonary osteoarthropathy. A common autonomic pathway could be postulated for most of these, but would meet with many difficulties by a chemical or a hormonal explanation. In the present cases simple division of the vagus produced relief of the pain and resolution of the œdema, although the pulmonary lesion was undisturbed. (It might be objected that the deep X-ray therapy to the primary lesion might have had an effect, but this is extremely unlikely because in case 2 the beneficial effects of the vagotomy were clear before the X-ray therapy was started.)

The complete relief of the pain and the disappearance of the œdema, despite the progression of the disease and the persistence of clubbing, appear, from the follow-up in these cases, to be permanent.

Many patients with hypertrophic pulmonary osteoarthropathy associated with an inoperable carcinoma of the bronchus might receive much benefit from vagotomy (which might be done through a thoracoscope).

Probably all patients undergoing thoracotomy for inoperable carcinoma of the bronchus, should also undergo routine vagotomy on the side of the lesion, irrespective of whether they have osteoarthropathy at the time or not.

In this way patients who have, or may have, one of the most painful manifestations of carcinoma of the bronchus may be saved a great deal of pain and discomfort and will therefore be able to spend several months of active life.

Summary

Two patients with inoperable pulmonary carcinoma and severe hypertrophic pulmonary osteoarthropathy treated by vagotomy obtained immediate complete relief of disabling pain. Associated œdema and, in one case, gynæcomastia also disappeared.

The possible mechanism of hypertrophic pulmonary osteoarthropathy is discussed, and a nervous reflex is favoured.

Despite the fact that this condition is rare, patients who undergo thoracotomy for an unresectable carcinoma of

the bronchus should have a vagotomy on the side of the lesion done as a routine. In inoperable cases with hypertrophic pulmonary osteoarthropathy this should be done where possible. By this relatively minor operation these patients will not only be saved much pain and misery but will also possibly live many months of active life.

We are grateful to Prof. B. W. Windeyer, Mr. T. Holmes Sellors, Miss M. D. Snelling, Mr. J. R. Belcher, and Dr. A. M. Jelliffe for permission to publish these cases, and we wish to thank Mr. M. Turney and the staff of the photographic department of the Middlesex Hospital for their invaluable help with the illustrations.

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PENICILLIN SENSITIVITY IN PATIENTS WITH BURNS

MARY R. DAVIES
M.B. Edin.
RESEARCH REGISTRAR, MEDICAL RESEARCH COUNCIL
BURNS RESEARCH UNIT, BIRMINGHAM ACCIDENT HOSPITAL

WITHIN recent years there have been a number of deaths from penicillin therapy (Wilensky 1946, Waldbott 1949, *British Medical Journal* 1951, Thompson 1952, Harpman 1952, Kern and Wimberley 1953, Feinberg and Feinberg 1956) and an increase in sensitivity reactions (*Lancet* 1957). The reported incidence has varied from 1·2% (Lepper et al. 1949) to 60·5% (Cornia et al. 1945), but 5–6% seems to be the usual reaction-rate following intramuscular injection (Mayer et al. 1953, Feinberg and Feinberg 1956). Detailed reports of reactions following local application of penicillin are few, but Kern and Wimberley (1953) stated that it leads to sensitivity more commonly than any other mode of administration; and figures of 10–20% have been cited (Templeton et al. 1947). By contrast, Collier (1958) found no sensitivity reactions in about 11,000 minor burns and wounds treated with penicillin ointment.

Penicillin cream has been used as the routine treatment for burns at the Birmingham Accident Hospital since 1945. It was introduced as a result of the observation in Glasgow that penicillin cream was efficacious against hæmolytic streptococcal infection of burns (Clark et al. 1943); and it has been proved to have considerable prophylactic value against the same organism (Jackson et al. 1951).

In the past, sensitivity reactions to local penicillin in this unit have been few and transient (Bull et al. 1954); but, in view of the reported increasing incidence of sensitivity reactions, the risks involved in the continued use of local penicillin have been freshly assessed.

Method

All patients were reviewed who attended the burns unit for the first time between Jan. 1 and June 30, 1957. The clinical staff were informed of the intended survey and recorded any possible allergic reaction. The use of 1% cetrimide as a cleansing agent was discontinued for the period of the review, since it can also cause sensitivity.

Penicillin cream was made in the following base:

Ol. ricini	28%
'Lanette Wax S.X.'	14%
Glycerin.	10%
Aqu. ad	100

TABLE I—FORMS OF PENICILLIN TREATMENT

Form	Inpatients	Outpatients	Total
Cream	82	1046	1128
Powder	49	266	315
Spray	25	10	35
Jelly	0	8	8
Eye ointment	1	1	2
Oral	7	6	13
Intramuscular	15	26	41
No. receiving more than one form	59	197	256
Total	120	1166	1286

The usual concentration of penicillin was 1000 units per g., but some patients had 10,000 units per g. for treatment of streptococcal infection. Penicillin powder was made up in a lactose powder base (10,000 units per g.).

1419 new patients attended during the six-month period. Of these, 1260 were outpatients, 135 were inpatients, and 24 were treated initially as outpatients and were admitted later. This last group has been included with the outpatients, since most of the penicillin cream was applied before admission. 436 outpatients (34%) and 68 inpatients (50%) were under 14 years of age.

1286 patients received penicillin during treatment, most of them having it locally (table I).

Results

Reactions

No anaphylactic reaction occurred. In 35 cases a rash developed. In some patients this was obviously due to a cause other than penicillin (for example, measles), but in 10 patients it was considered on clinical grounds that the rash might be a penicillin sensitivity reaction (table II). Other possible sensitising agents had been given to four of these patients—namely, plasma (3), blood (1), streptomycin (1), and a jelly of unknown composition (1). 4 of the reactions followed the systemic administration of penicillin (3 intramuscularly, 1 orally) combined with local therapy. In the majority the rash occurred twelve to sixteen days after burning; in 3 it occurred on the fourth to fifth days; and in the remaining patient on the twenty-second day a few hours after the first injection of penicillin. No rash lasted longer than four days, and in the majority it subsided within forty-eight hours. 6 of the 10 patients had penicillin cream applied again, three days to six months later, with no reaction.

Only 1 patient had any systemic upset accompanying the rash.

This patient sustained an 8% burn of face and hands. The hands were dressed with penicillin cream and the face was treated by exposure with penicillin powder. The dressings were changed on days 1, 4, 11, and 14. On the evening of day 14 an urticarial rash developed on the legs and trunk. The patient was given mepyramine 100 mg. t.d.s., and calamine lotion was applied locally. The following day the rash continued; she complained of abdominal pain and vomited twice. On day 16 the dressing was changed to tulle-gras, and the rash faded. Skin-grafting was carried out on day 19 and tulle-gras dressings were continued. On day 31, group-A hæmolytic streptococci were found on the hands, which were then dressed with penicillin cream 10,000 units per g. This dressing was repeated on days 32, 34, 36, 37, 39, and 40. There was no reaction to these later applications.

2 other patients had a definite allergic reaction; but as neither had received penicillin in any form the reaction could not be attributed to this cause.

If the rashes have been correctly attributed, then the total incidence of penicillin reactions was 0·8% (10 out of 1286). The incidence in inpatients was higher (3·3%) than in outpatients (0·5%). Although this could be due to more extensive application of the cream, it seems more

TABLE II—RASHES IN 1419 PATIENTS

Type of reaction	Inpatients	Outpatients	Cause to which rash attributed				No penicillin before rash	"Penicillin" rash; no reaction to later penicillin
			Penicillin	Infection	Irritation	Other		
Urticarial with systemic upset	1	0	1	..	..	..	..	1
Urticarial only	3	1	4	..	..	..	..	3
Measles	4	0	..	4	..	..	..	..
Chickenpox	1	0	..	1	..	..	..	..
Scarlatinaform with hæmolytic streptococcal infection	2	1	..	3	..	..	1	..
Generalised erythematous (other than above)	2	5	4	1	..	2*	2	2
Localised	3	12	1	4	10	..	2	..
Total	16	19	10	13	10	2	5	6

* 1, tulle-gras; 1, blood-transfusion.

likely to be the effect of a larger number receiving systemic therapy. The overall incidence of reactions in those receiving local application only was 0·5% (6 out of 1232); and in those having systemic therapy, usually combined with local, 7·4% (4 out of 54).

Since a number of outpatients had minor burns and did not attend hospital more than once or twice, these figures may be falsely low. 203 outpatients receiving penicillin were transferred, or did not attend more than twice. If, for this reason, these patients are excluded, then the total incidence of reactions was 0·9% (10 out of 1083); in outpatients 0·6% (6 out of 963); from local application only 0·6% (6 out of 1030); from combined systemic and local administration 7·6% (4 out of 53).

History of Previous Sensitivity

14 outpatients (1·1%) and 3 inpatients (2·2%) gave a history of allergy to penicillin. 7 of these had penicillin cream applied during treatment, and none had a reaction.

One patient with a history of penicillin sensitivity had a reaction.

This patient had penicillin injections on account of a septic finger in 1955. Eighteen months later (December, 1956) he sustained a 1·5% burn of the forearm, which was treated with penicillin powder and boracic fomentations at work. When he was referred here two weeks after injury, the area was rather swollen. Penicillin cream was applied, and three days later he had a sensitivity reaction. The dressing was changed to tulle-gras; but he returned the following day with the arm more swollen and painful, and a vesicular eruption over the whole burned area. The reaction gradually subsided with local calamine lotion and systemic antazoline. In June, 1957, he sustained a small burn of the opposite forearm. This was dressed with tulle-gras, and two days later he returned with swelling of the forearm and a vesicular rash over the area covered with tulle-gras. The rash and burn healed in two weeks. It is apparent that this patient was sensitive to tulle-gras which he had on both occasions, as well as to penicillin.

Discussion

In assessing the incidence of penicillin sensitivity, the first difficulty is correct diagnosis. Where patients are exposed to several possible sensitising agents, this may be extremely difficult. Skin tests are generally considered to be unreliable (Farmer 1953, Tuft et al. 1955, Feinberg and Feinberg 1956) and penicillin sensitivity may be lost spontaneously (Matthews et al. 1956). 6 of our patients with "penicillin sensitivity" had no reaction to repeat applications within six months; either they must have lost their sensitivity very rapidly, or the reaction was wrongly attributed to penicillin. Similarly, of the 17 patients who gave a history of previous allergy, 7 were exposed to the drug with no reaction.

None of the reactions in these patients endangered life, nor are we aware of any serious reaction during the thirteen years the drug has been used routinely here. Most of the reactions were mild and transient, and some would not have been noted had the review not been in progress. Only a few patients had any appreciable discomfort from the reaction.

Comparing the incidence of reactions in this series with other published results, the reaction-rate after systemic administration (7·4%) is of a similar order to that found by other workers (Lyons 1943, 5·7%; Mayer et al. 1953, 6%; Vickers et al. 1958, 5%). Our incidence after local application only (0·5%) is much lower than other reported figures. Reports of reaction to local therapy have usually been on patients with dermatitis, who are probably particularly susceptible (Kolodny and Denhoff 1946). The present results, in patients without skin disease, show a very low reaction-rate to local application of penicillin, and much lower than to systemic administration.

The necessity of incurring even this small risk may reasonably be questioned, and there would be no justification if there was another agent which was as effective and safer. Local penicillin cream is at present the best prophylactic agent against colonisation with *Streptococcus pyogenes*, which so frequently causes graft failure. In a controlled trial of cases of burns, *Str. pyogenes* infection developed in only 3·7% of cases treated with penicillin cream, compared with 47·4% in a control group (Jackson et al. 1951). In view of its obvious advantages and the low incidence of reactions penicillin cream can justifiably be applied prophylactically.

Summary

1419 patients with burns were observed for evidence of any sensitivity reaction.

0·5% (6 out of 1232) of patients receiving local penicillin had a reaction possibly attributable to penicillin; compared with 7·4% (4 out of 54) of patients receiving systemic penicillin. Most of the reactions were mild, and none lasted longer than four days.

Accurate diagnosis is often difficult; and the sensitive state may be transient, as is illustrated by the fact that 6 of the 10 patients with "penicillin sensitivity" had no reaction to subsequent local application of the drug.

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ANXIETY STATES FOLLOWING VESTIBULAR DISORDERS

R. T. C. PRATT
M.A., D.M. Oxon., M.R.C.P., D.P.M.
PHYSICIAN IN PSYCHOLOGICAL MEDICINE

WILLIAM MCKENZIE
B.A., M.B. Cantab., F.R.C.S.
OTOLOGIST

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, LONDON, W.9.

DISTURBANCES of balance resulting from vestibular disorders have long been known to lead to severe anxiety (Gowers 1893, Cawthorne 1957). The recent finer analysis of affections of the eighth nerve, in particular by Hallpike and his colleagues (Cawthorne et al. 1956, Carmichael et al. 1956), has led to improved diagnosis of these patients. The factor of positional nystagmus of the benign paroxysmal type in causing some of the symptoms of the post-traumatic state has been emphasised (Gordon 1954, Harrison 1956), together with the importance of differentiating these symptoms from those of psychological origin. Less attention has been paid to the mental features displayed by patients with disturbances of balance.

On the other hand, complaints of disturbance of balance are a classical feature of hysteria and anxiety states (Mayer-Gross et al. 1954) and are then generally accepted as being without organic basis. We review here 12 cases (see table) in which anxiety states followed directly on disturbance of balance and the symptoms attributable to anxiety predominated. The prognosis of these anxiety states appeared to depend on the recognition and treatment of the primary disturbance.

Illustrative Case-reports

Case 1.—A clerk and housewife, aged 24, developed attacks of unsteadiness, feeling " as if mildly drunk " and as if she had just been subjected to rotation, brief initially but later more persistent, and increasingly accompanied by panic attacks, depression, fears of dying, and a feeling of vibration in the head with preoccupation about her symptoms. (She had no rotatory vertigo until six months after the onset.) She had previously been free from neurotic symptoms, apart from a tendency to worry. When seen five weeks after the onset caloric responses were minimal. No diagnosis, however, could be made by otological examination. She improved slowly at first with sedation and reassurance, and more rapidly when she was instructed in a range of balancing exercises seven weeks after the onset. She returned to work six weeks later, and her symptoms continued to improve. When seen six months after the onset her caloric responses showed no change; she reported that this test led to rotatory vertigo followed by her non-rotatory unsteadiness. A year after the onset she had been symptom-free for five months.

Case 3.—A male factory worker, aged 43, had had occasional attacks of vertigo lasting up to five minutes since the age of 12 years. He had rotatory vertigo if the attacks came on when he was lying down, but in the erect position his surroundings seemed to tip to the right. Of late he had become increasingly fearful of an attack, was never at ease sitting in a cinema even when at the back in the end seat, and felt particularly tense in the barber's chair. In addition, apart from his attacks, for a month or so he would feel that he must walk on the left side of the pavement, and used to sweat if he had to walk on the right side. He was adopted, had an unhappy childhood, walked once in his sleep, wet the bed until the age of 6 years, and occasionally stammered when flustered. His caloric responses were normal but reproduced the sensation of vertigo. No otological diagnosis was made. He had not improved on anticonvulsants, but improved promptly when he was instructed in a range of balancing exercises. His attacks of vertigo became somewhat less frequent, his feelings of anxiety vanished, and he reported that he was still well in this respect a year later.

Case 12.—A housewife and hairdresser, aged 38, reported that, nine months previously, after a period of overwork, she developed a muzzy feeling with continuous headaches and depression, and three months later spent three weeks in bed feeling exhausted; during this time she had a continuous feeling that she was falling through the bed. She had previously been free from neurotic symptoms. She continued to be depressed and to have dizziness and nausea, and did not improved with sedation and superficial psychotherapy. Seven months after her first attendance she reported an attack in which her surroundings went round and round and she staggered; she then recalled that she had had this sensation fifteen months before her first attendance and earlier than that for very brief periods. On otological examination her caloric responses were normal, apart from a minimal response to water at 44°C in the right ear, but she reported that the sensation she had experienced during irrigation was similar to her spontaneous dizziness and nausea. No otological diagnosis was made. She was then given bending exercises and promethazine chlorotheophyllinate (' Avomine ') 25 mg. t.i.d. and reported an immediate improvement in her dizziness, maintained during follow-up.

Symptoms

Of the 12 patients 8 (see table) had episodes of frank rotatory vertigo, usually of brief duration. Case 5 had paroxysmal nystagmus of the benign positional type.

Non-vertiginous symptoms attributable to vestibular disorder occurred in 9 patients and were described variously as giddiness, dizziness, unsteadiness, or impairment of balance. In 5 patients (cases 4, 6, 8, 10, and 12) these symptoms were worse on movement, in case 2 after getting off a bus or a train, and in case 9 only during rapid movement of the head.

Of the psychological symptoms the most common were panic attacks (7 patients), fears of travelling (5 patients), reactive depression (5 patients), feelings of tension (3 patients, in 2 of whom it was particularly severe in the barber's chair), and exhaustion (2 patients).

Treatment

An explanation that the primary disorder is an organic affection of the balancing mechanism often affords great relief to the patient, who may have been fearing insanity or a grave organic disorder. Balancing exercises not only give confidence but also appear to hasten the disappearance of feelings of unsteadiness. Three forms of balancing exercise were given, the simplest (cases 4, 5, 7, 11, and 12) being putting the head between the knees from a standing position ten times in succession, to be repeated several times a day (" bending exercises "). A full range of balancing exercises, from eye and head movements to vigorous bending (Cawthorne 1946, Cooksey 1946), was given to some of the patients, and was continued either at home (by cases 1, 3, 9, and 10) or in the physiotherapy department (by cases 2, 6, and 8). The simple bending exercises may suffice, but better results were obtained with the full range of balancing exercises. Sedatives by day or night

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ANALYSIS OF CASES

Case no.	Sex	Age (yr.)	Duration vestibular disorder (yr.)	Rotatory vertigo	Non-rotatory vestibular symptoms	Reproduction of vertigo (V) or non-rotatory vestibular symptoms (1) by caloric test	Anxiety symptoms		Previous neurosis (severity 0–3)	Duration of follow-up after first being seen (yr.)	Progress after treatment
							Severity (1–4)	Duration (yr.)			
1	F	24	1/12	Late	+	V+1	4	1/12	1	1	Recovered
2	M	52	11	—	+	1	4	6	1	2½	,,
3	M	43	31	+	—	V	2	5	1	1	,,
4	M	43	9/12	—	+	—	4	9/12	2	5/12	Improved
5	F	57	27	+	+	V	4	27	1	11/12	,,
6	M	28	7	+	+	—	4	2	1	2	Recovered
7	F	26	6/12	+	—	—	2	6/12	0	6/12	,,
8	F	16	9/12	—	+	?	4	6/12	3	6/12	I.S.Q.
9	M	40	2	+	+	V	1	6/12	1	1⅔	Recovered
10	F	28	6/12	—	+	1	4	9/12	0	7/12	Improved
11	F	25	1⅔	+	—	V	3	1⅔	0	1	I.S.Q.
12	F	38	1⅔	+	+	1	3	9/12	0	9/12	Improved

were given when they seemed required, but cases 7 and 9 recovered when bending exercises were introduced and sedatives stopped. Antihistaminics were given to 5 patients (dimenhydrinate 50 mg. t.i.d. in cases 4, 5, 10, and 11, and promethazine chlorotheophyllinate 25 mg. t.i.d. in case 12) at the same time as exercises, and any independent effect they may have had could not be determined.

Discussion

Vertigo has long been known to cause anxiety and the fear of further attacks. On the other hand, complaints of unsteadiness, subjective and objective, are a classical feature of anxiety states and hysteria. The present patients were all considered to have a vestibular disorder, 4 without rotatory vertigo and 3 without symptoms of unbalance between their attacks of vertigo. In all the patients the outstanding and disabling symptoms were attributable to anxiety consequent on the vestibular disorder. Usually those without previous neurotic traits were less severely affected as regards their anxiety symptoms, as would be expected, but their outcome was no better. Absence of rotatory vertigo was an unfavourable prognostic symptom. 3 patients (cases 2, 5, and 12) had had long periods of psychiatric treatment without any improvement until the organic basis of their disability was recognised. The response to treatment by explanation and exercises was encouraging, 6 patients becoming free from anxiety, and 4 others showing definite improvement.

From the otologist's point of view these cases present considerable difficulty. The tests for vestibular disturbance are still relatively undeveloped, and while the differential caloric test of Fitzgerald and Hallpike (1942) is most helpful it cannot provide conclusive evidence in every case. The difficulties of the test are well known: the test needs an expert to apply it, and the margin of error of the test should lead to reserve about its interpretation in the absence of other signs. In vestibular neuronitis there may be a complete lack of vestibular response on one side, whereas the other may be normal, and in this event a diagnosis can be made with certainty. On the other hand, the equally well-known condition of benign paroxysmal nystagmus, when transient vertigo develops with the head in certain positions, may be associated with a normal response to the differential caloric test. In benign paroxysmal nystagmus the signs may wax and wane, so that a patient may have this disease and yet, if his visit to hospital coincides with a period of freedom, may show no sign to the examiner. The possibility, therefore, that a patient with this disorder may be thought to be entirely neurotic should make for hesitation in assessing a patient who is described as a victim of vertigo. These patients should certainly be examined as thoroughly as possible, and it is a reasonable suggestion that no one who can complain in detail of an apparent movement of objects should be considered neurotic. Whether this complaint can be confirmed by objective evidence is uncertain; it clearly can sometimes, but there is often doubt because the available vestibular tests are not sufficiently accurate. That a patient with an established disorder—such as Ménière's disease—can develop a neurosis is equally well known. All otologists will know of patients with Ménière's disease who were considered to be neurotic, simply because the neurosis which had developed was so obvious that it concealed the Ménière's disease. There is no reason why this should not happen in other vestibular disorders, and in future more precise methods of examination may supply proof of organic disease in patients who would otherwise be considered neurotic.

The caloric responses of the present patients cannot be attributed to anxiety, because they differ from those found by Hallpike et al. (1951) in 35 patients with severe anxiety neurosis, who showed greater overall sensitivity with a greater degree of variance than did a healthy group.

Our patients were extracted from 466 consecutive patients without organic disease of the central nervous system referred to one of us (R. T. C. P.) for psychiatric opinion by the physicians of the neurological hospital over a period of three years. Thus the syndrome appears to be common, although it may be over-represented in the material of a neurological hospital.

The association between vertigo and endogenous depression is also of interest. Of 146 patients with endogenous depression seen over the past three years at this hospital, in 14 a complaint of vertigo was made and was considered to have a basis in an organic vestibular disorder. In 10 of these patients the attacks of vertigo and of depression were independent, in 3 the onset of vertigo led directly to a recurrence of a depressive state, and in 1 the onset of vertigo led to the initial attack of endogenous depression. It is therefore possible that vestibular disorders may be counted among those physical illnesses incriminated by Roth and Kay (1956) as responsible in some patients for the precipitation of an attack of endogenous depression.

Summary

An account is given of 12 patients in whom anxiety states directly followed disturbances of balance and in whom the symptoms attributable to anxiety predominated.

The prognosis of these anxiety states depended largely

on recognition of the primary disorder and on treatment by balancing exercises.

We wish to thank our colleagues at Maida Vale Hospital for referring these patients to us, and Dr. Eliot Slater and Dr. Alick Elithorn for their advice and criticism.

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ACUTE RENAL FAILURE DUE TO MUSCLE NECROSIS IN CARBON-MONOXIDE POISONING

LAVINIA W. LOUGHRIDGE
M.B. Belf., M.R.C.P.
REGISTRAR, DEPARTMENT OF MEDICINE,
POSTGRADUATE MEDICAL SCHOOL, LONDON, W.12

LESLEY P. LEADER
M.B., B.Sc. Lond., M.R.C.P.
REGISTRAR, WEST MIDDLESEX HOSPITAL, ISLEWORTH, MIDDX.

D. A. L. BOWEN
M.A., M.B. Cantab., M.R.C.P.E., D. Path.
DEMONSTRATOR, DEPARTMENT OF FORENSIC MEDICINE,
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, LONDON, S.W.1

SKELETAL muscle necrosis leading to acute tubular necrosis of the kidneys is a rare complication of carbon-monoxide intoxication.

Günther (1921) recorded fatal renal damage, with oliguria, in an adult male following eleven hours' coma due to exposure to carbon monoxide in a cold atmosphere; an abnormal pigment, described as hæmatoporphyrin, was found in the urine. The necropsy findings in the same case (Scharmann 1921) revealed degeneration of the muscles in the areas affected by postural pressure.

Hedinger (1948) reviewed 30 cases of muscle necrosis in carbon-monoxide poisoning; the affected muscles were painful and swollen, and in 12 cases histological confirmation was obtained.

In Fowler's (1954) case of gangrene in a lower limb, following carbon-monoxide poisoning, peripheral vascular disease was probably an important factor. The patient, a man aged 58, had a previous history of intermittent claudication, and his femoral artery, on amputation, showed gross atheroma with medial calcification. No reference was made to renal lesions in this case.

Mautner (1955) described a case of attempted suicide with carbon monoxide, in which temporary oliguria with a non-protein-nitrogen level of 85 mg. per 100 ml. was associated with brawny œdema of the right shoulder, upper arm, and thorax, and muscle necrosis was found on biopsy. Mautner credits Larrey (1812) with the first description of muscle necrosis in carbon-monoxide poisoning. Probably, however, the sacral and scapular lesions were superficial pressure sores rather than areas of muscle necrosis. There was no reference to renal lesions in these cases.

The present paper records the clinical and pathological findings in a fatal case of acute tubular necrosis of the kidneys following myonecrosis in coal-gas poisoning, and emphasises the importance of frequent clinical and laboratory assessment of such cases in view of the particular biochemical hazards in renal failure from this cause.

Case-report

A female Indian student, aged 23, was found unconscious in a gas-filled room on Sept. 24, 1957. On admission to hospital an hour later she had recovered consciousness but complained of pain in her back and in both legs.

On examination she was an obese girl of healthy appearance, who made no spontaneous movements of either leg and had a variable degree of hypoæsthesia to pinprick. Direct questioning revealed no history of suicidal intent, the accident having occurred through ignorance of the mechanism of gas-heating. She had probably been unconscious for at least seven hours, and the position of her lower limbs on discovery suggested an initial squatting posture.

Progress.—Next day she vomited several times and passed less urine (not accurately recorded). Within the next twenty-four hours she passed only 180 ml. of urine, and on Sept. 27 her blood-urea level had risen to 163 mg. per 100 ml. Her blood-pressure was 115/80 mm. Hg, and she had no anæmia. Gynæcological examination revealed no abnormality. No past history of renal disease, diabetes, or exposure to known renal toxins was obtained. Catheterisation of the bladder on Sept. 28 produced 90 ml. of urine with Sp. gr. 1·016 and moderate proteinuria but no glycosuria. Conservative treatment of acute renal failure was instituted with hypertonic dextrose solution administered through a polyethylene catheter into the superior vena cava.

On Sept. 30 an extensive soft-tissue swelling, with œdema of the overlying skin, was observed to involve the inner side of the right thigh and to extend above the inguinal ligament. There was extreme local tenderness but no superficial bruising. Limitation of internal rotation at the right hip-joint was present, and the limb was held in a position of external rotation. There was, however, no shortening of the leg. Tendon-reflexes were absent on the right side, and neither plantar response could be elicited. Appreciation of pinprick was impaired, but a segmental distribution could not be defined.

At this stage, six days after the onset of oliguria, acidotic breathing was noted, though the patient remained fully conscious, with blood-pressure 120/85 mm. Hg, optic fundi normal, and both kidneys enlarged and tender. The blood-urea level had risen to 325 mg. per 100 ml. and the serum-potassium level to 5·9 mEq. per litre. Electrocardiography showed minimal peaking of T waves in precordial leads. There was a significant acidæmia, with serum-bicarbonate level 16·9 mEq. per litre. The hæmoglobin level was 13·9 g. per 100 ml., white blood cells numbered 4000 per c.mm., and the erythrocyte-sedimentation rate was 12 mm. in the first hour (Westergren). Radiography of the lumbosacral spine and hip-joints was normal.

On Oct. 1 the patient passed only 90 ml. of urine. Her blood-urea level was 335 mg. per 100 ml., serum-potassium level 6·8 mEq. per litre, and serum-bicarbonate level 12.8 mEq. per litre. Soluble insulin was added to the intravenous infusion, and an attempt was made to give ion-exchange resin by mouth though vomiting was still frequent. On Oct. 2, although the blood-urea level had risen to 470 mg. per 100 ml., the patient's general condition was satisfactory and vomiting less troublesome. There was no impairment of consciousness, and she could now move the affected leg, which, however, was still swollen. Her serum-bicarbonate level remained at 12·7 mEq. per litre, and her serum-potassium level was 7·0 mEq. per litre. Preparations for hæmodialysis with an artificial kidney were being made, when the patient collapsed suddenly at 6 A.M. on Oct. 3 with impalpable pulse and unrecordable blood-pressure and died within a few minutes.

Necropsy findings.—The body was that of a well-built obese young Indian woman. The upper third of the right thigh appeared swollen, and incisions into it revealed œdema of the

subcutaneous tissues. The underlying adductor-muscle group, for about twelve inches of its length, was abnormally pale, yellowish-grey, and patchily mottled. Some areas presented a "fish-flesh" appearance. The muscles of the other limbs showed no abnormality. The meninges and cerebral hemispheres were congested, and the brain was œdematous. The heart was normal in size, with healthy valves, coronary arteries, and aorta. There were bilateral terminal congestive changes in the lungs, with a normal pulmonary arterial tree. Acute congestion of the liver was present. The kidneys were pale and swollen, weighing 210 and 220 g. The tense capsule stripped readily from the renal substance, and the cortex was pale, moist, and increased in width. The medulla was mottled dusky red, and its junction with the cortex was indistinct. There was no occlusion of the renal vessels. The uterus and adnexa appeared healthy.

Histology.—Sections from the affected muscle revealed changes varying from loss of striation to complete degeneration of fibres (fig. 1). Most fibres appeared waxy, with fragmentation, vacuolation, and shrinkage of degenerate sarcoplasmic remnants. In some areas phagocytosis of dead muscle by histiocytes was seen, while elsewhere empty sarcolemmal sheaths were evident. Areas of hæmorrhage between the muscle bundles were prominent in one section. There was interstitial œdema with invasion by polymorphs, eosinophils, and lymphocytes. No calcification was seen. Many arterioles showed fibrinoid necrosis with intraluminal thrombi in some instances. There was much perivascular cuffing with polymorphs and mononuclear cells. There was no abnormality of the larger vessels. Sections of the kidneys revealed glomeruli which were normal apart from an eosinophil coagulum in some of the capsular spaces (fig. 2). The distal convoluted and collecting tubules contained dense benzidine-positive casts. Some of the proximal tubules were intact, but others were dilated and lined by flattened regenerating epithelium. There was some œdema of the interstitial tissue, with infiltration by chronic inflammatory cells, and in the cortex there was evidence of a focal perivascular histiocytic reaction adjacent to ruptured tubules. Sections of blood-vessels from other organs in the body showed no abnormality.

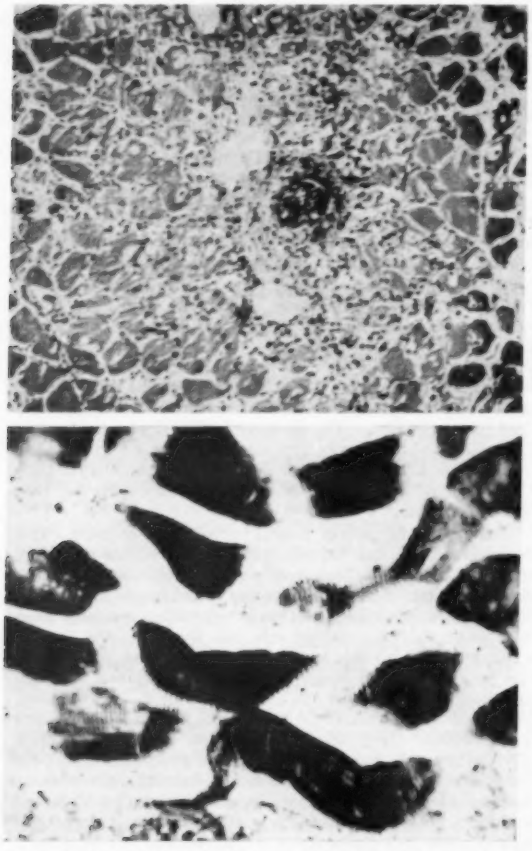

Fig. 1—Section of adductor muscle showing: upper part, disruption of fibres, arterial necrosis, and cellular infiltration (hæmatoxylin and eosin, ×93); lower part, loss of striation (phosphotungstic acid hæmatoxylin, ×177).

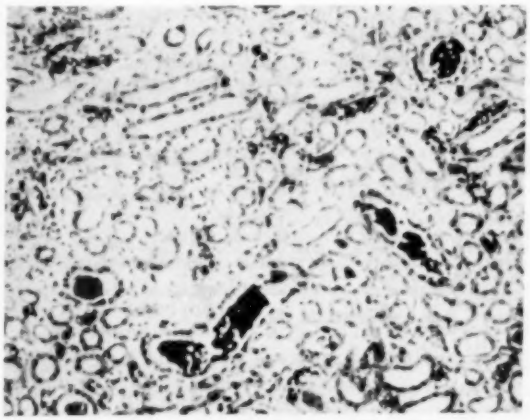

Fig. 2—Section of kidney showing tubular casts and regenerating epithelium (hæmatoxylin and eosin, ×158).

Discussion

The association of myoglobinuria with acute tubular necrosis of the kidneys is well recognised. Myoglobinuria results from damage to skeletal muscles, of which the main causes, in man, are trauma and Haff disease (Hed 1955). The latter condition, believed by some to be a seafood allergy, has been reported mainly in East Prussia. Other non-traumatic causes, listed by Hed, include arterial occlusion with ischæmia, convulsions, myositis, muscular dystrophy, and paroxysmal myoglobinuria without progressive muscular dystrophy. The traumatic group comprises crush injuries, high-voltage shocks, and localised muscle necrosis due to postural pressure.

In the present case muscle necrosis followed seven hours' exposure to carbon monoxide, with presumed immobilisation of the patient, and was restricted to a localised area of one leg. Probably the combined factors of local ischæmia due to pressure, particularly in an obese person, and anoxæmia, due to carbon monoxide, were responsible for the muscle damage. The importance of decreased arterial oxygen, due to carbon monoxide, has been emphasised; perhaps in such cases the gas interferes directly with the oxidative enzymes of muscle by forming carboxymyoglobin. Histologically there was no evidence of generalised arterial disease, sections of vessels from other organs being quite normal.

Pressure necrosis of muscle has been reported to follow unconsciousness due to other agents, including alcoholism, alcoholism plus "sleeping tablets" (Jasinski and Brütsch 1952), barbiturates (Touzé and Thierry 1952), alcoholism plus barbiturates (Fahlgren et al. 1957), and general anæsthesia (Gordon and Newman 1953). In some of the published cases the patients were obese, and the assump-

tion of an abnormal posture during immobilisation has been emphasised.

Most of the published cases of muscle necrosis following prolonged coma have been followed by acute renal failure. In some such cases myoglobin pigment was found in the urine during life, whereas in others pigment casts in the renal tubules were found at necropsy. In the present case myoglobinuria was not found, but the typical casts were present in the kidneys. The histological findings were those of acute tubular necrosis, the large numbers of casts in the collecting tubules, some interstitial reaction, polymorph invasion of casts in the cortical zone, and evidence of regeneration of tubular ephithelium being consistent with a duration of ten days. There was no evidence of antecedent renal disease.

Early recognition of renal involvement in cases of muscle necrosis is important for the institution of a suitable regime for treating acute tubular necrosis of the kidneys. Exact diagnosis depends on the spectroscopic demonstration of myoglobin in the urine; but, since this is early and probably transient, it is unlikely to be found at the stage of clinical renal failure. It is important to exclude muscle necrosis in patients developing acute renal failure after coma, particularly where it is associated with anoxæmia. A suspected clinical diagnosis can be confirmed or refuted by muscle biopsy.

The renal lesion associated with muscle necrosis is potentially reversible, but the biochemical hazards, in particular that of sudden hyperkalæmia, seem less predictable than in tubular necrosis from other causes—e.g., ischæmic "shock" and drugs. Of Falhgren's (1957) 5 patients with myonecrosis and myoglobinuria following alcohol and barbiturate poisoning 2 died from hyperkalæmia. Hed's (1955) patient with renal failure, following the allied idiopathic condition of paroxysmal myoglobinuria, died with a serum-potassium level of 12·3 m.Eq. per litre and gross electrocardiographic evidence of hyperkalæmia. In the present fatal case the cause of death was presumed to be a further sudden rise in serum-potassium level above the last recorded figure of 7·0 m.Eq. per litre. It is imperative, therefore, that such cases should have at least twice-daily estimations of serum electrolyte levels, particularly potassium, and electrocardiography. Where possible they should be transferred, at an early stage, to a centre where hæmodialysis is available, if control by conservative therapy seems unlikely to prove adequate. Dialysis should be considered at a relatively lower level of serum-potassium than is customary, in view of the great risk of further sudden releases of this cation into the circulation as muscle breakdown continues.

In conclusion, it is emphasised that the cause of this accident was the victim's ignorance of the mechanism of gas-heating. Visitors from overseas who are unfamiliar with the use of coal-gas should be instructed in its dangers.

Summary

A case of fatal renal damage following skeletal muscle necrosis in carbon-monoxide intoxication is described. The clinical course was that of acute, oliguric renal failure with terminal hyperkalæmia.

Postmortem examination revealed extensive muscle necrosis in one lower limb, and the changes of acute tubular necrosis with pigment casts in the kidneys.

Our thanks are due to Dr. G. L. B. Thurston, H.M. Coroner, London, West District, Dr. M. D. Milne, and Dr. N. F. Coghill for advice and permission to publish; and to Prof. T. Crawford for the photomicrographs.

References at foot of next column

Preliminary Communication

SELECTIVE PLACENTAL TRANSFER OF SERUM-PROTEINS IN THE RHESUS

THE transfer of antibodies from mother to young before and after birth has been studied in many laboratory animals and in man.[1] Nearly all the evidence for their transmission to the fœtus has been based on immunological studies comparing the titre of specific antibodies in maternal blood with their titre in fœtal or cord blood. Although it has been assumed that in man their transfer is directly via the placenta, comparative studies in orders other than the primates have led Brambell et al.[2] to suggest that the route in primates may be via the amniotic fluid, selection of γ-globulins taking place at the entodermal lining of the fœtal gut.

The transmission of other serum-proteins from mother to fœtus has received little attention. Whipple et al.[3] studied the transfer of ^{131}I-labelled serum-proteins in rabbits and dogs. Labelled protein (unspecified) was found in the rabbit fœtuses but not in the dog. The transfer of heterologous albumin has been demonstrated in the rabbit, using immunological measurement.[4] So far, however, there has been no study of the transmission of homologous serum-proteins to the fœtus of any animal.

Since a hæmochorial placental system comparable to that of man is found only among the catarrhine and anthropoid primates, the problem in relation to man can be investigated only in Old World monkeys or in apes. The placenta of the rhesus (catarrhine) comes to resemble the human placenta very closely in the later stages of pregnancy.[5]

We present here evidence of the selective transmission of whole homologous serum-proteins from mother to fœtus in the rhesus monkey, and demonstrate that the amniotic fluid plays an unimportant part in the transfer of whole serum-proteins.

MATERIALS AND METHODS

Pregnant rhesus monkeys (*Macaca mulatta*) (B, C, D, and F) weighing 6–8 kg., and a green monkey (*Cercopithecus æthiops*) (E) weighing 5·2 kg., were used. The monkeys were estimated to be within 4–6 weeks of the end of their gestation period (6 months). A sample of their blood was taken, and they were then given iodide water (0·02% NaI) to drink ad libitum for 1–2 days before the experiment and throughout its duration. Of this sample 0·3 ml. of serum was iodinated with an average of not more than 1 atom of iodine per molecule of protein.[6]

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The doses prepared contained 1·6–1·8 mC of ^{131}I in 20 mg. of serum-proteins (350–400 million counts per min.), of which less than 2% was free iodide.

Undialysed serum-protein samples (1·0 ml.) were separated by electrophoresis in borate buffer (μ=0·05, pH 8·5) on treated cellulose columns. The columns (38 × 1 cm.) were developed for 8½ hours with 600 volts. The proteins were eluted with buffer in 2 ml. fractions. γ-globulins in unhæmolysed serum samples were isolated after dialysis against 0·02 M phosphate buffer (pH 6·2) on 1 g. columns of diethylaminoethyl cellulose (D.E.A.E.)[7] and eluted with buffer in 2 ml. fractions. Most serum and liquor samples were also similarly fractionated after passing through 'Deacidite' FF (Permutit Co., an anion exchange substituted polystyrine, 100–200 mesh, in sodium form) used to adsorb residual free iodide after iodination of the dose. Radioactivity was measured in a well-type scintillation counter with an efficiency of 16·2% for ^{131}I and a background of 130 c. per min. All samples were counted for a minimum of 4000 counts, except for very weak samples on column fractions which were counted for 1000 counts. The protein in each column fraction was measured at 280 mμ in a 'Unicam' spectrophotometer and then counted.

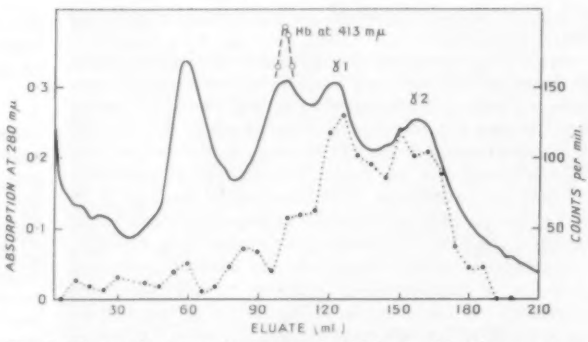

Fig. 3—Eluate of column electrophoresis of 1·0 ml. of fœtal serum (untreated) showing the presence of labelled γ1 and γ2 globulin 8 hours after the dose (monkey C).

Red blood-cells taken from the mother at the same time were labelled with 0·8–1·0 mC carrier-free ^{51}Cr for an hour at room temperature in acid citrate dextrose (A.C.D.). After washing thoroughly in saline (final activity = 37,000 c. per min. per mg. Hb) they were stored in A.C.D. at +4°C until use within 24 hours. Fœtal red cells were washed in saline (6 × 15 ml.) and 3 ml. of packed cells counted in the scintillation counter.

EXPERIMENTS ON TRANSPLACENTAL TRANSFER
(Monkeys B, C, and D)

Procedure

The ^{131}I-labelled serum was mixed with the ^{51}Cr-labelled red cells and injected intravenously into the mother. Anæsthesia was induced 8–9 hours later with thiopentone and maintained with cyclopropane in closed circuit or with open ether. The lower segment of the uterus was incised down to the level of the fœtal membranes, and through an avascular part 20–80 ml. of blood-free amniotic fluid was aspirated with needle and syringe. The fœtus was delivered and exsanguinated immediately by open heart puncture. A sample of maternal blood was taken just before or just after delivery of the fœtus.

Results

3 ml. of packed fœtal red cells gave a count not significantly above background, indicating that there had been no gross contamination with maternal blood due to accidental hæmorrhage in utero. Column electrophoresis of the ^{131}I-labelled dose in carrier serum indicated that, although the specific activity of the albumin peak was always 2–3 times the specific activity of the globulins, the count pattern followed the protein (absorption at 280 mμ) pattern closely. About 80% of the total counts were with the albumin, about 4% in the γ-globulin isolated chromatographically, and, by difference, about 16% in the other globulins. Fœtal serum (fig. 1) contained radioactivity in the albumin peak and γ-globulin-fraction peak. Some of the activity of the albumin appeared to be due to adsorbed free ^{131}I iodide, which was removed by deacidite FF (fig. 2). Dialysis for 48 hours in 5% NaI failed to reduce the specific activity any further. There were almost as many counts in the γ-globulin as there were in the albumin, indicating that

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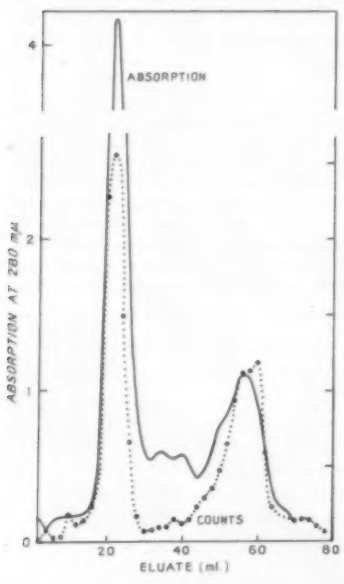

Fig. 1

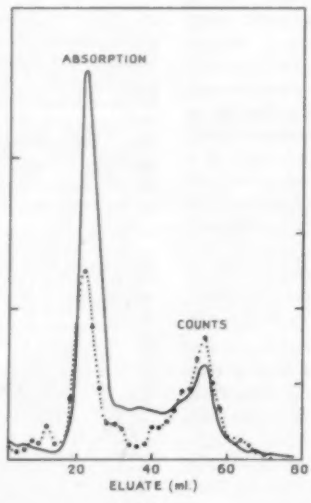

Fig. 2

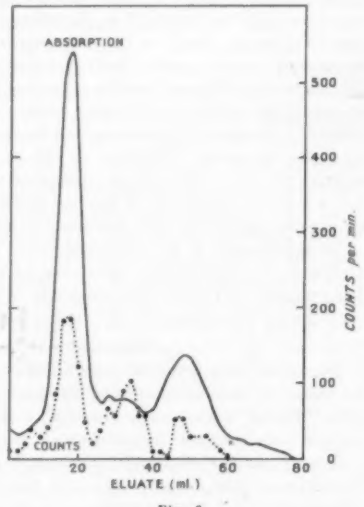

Fig. 5

Figs. 1 and 2—Eluate of column electrophoresis of 1·0 ml. of fœtal serum untreated (fig. 1) and after treatment with deacidite FF and dialysis against 5% NaI and 0·01% monoiodotyrosine (fig. 2). (Monkey D, 8 hours after the dose.) This shows the presence of radioactive albumin and γ-globulin (dotted line

Fig. 5—Eluate of column electrophoresis of 1·0 ml. fœtal serum after treatment with deacidite FF (monkey F), 24 hours after injecting into the amniotic fluid the same amount of radioactive serum-proteins as was used for transplacental experiments B, C, and D. There is little absorption of any specific labelled protein.

γ-globulin was transmitted to the fœtus some 15–20 times more easily than albumin. Moreover, the γ-globulin isolated by D.E.A.E. chromatography accounted for almost all the counts in the β and γ globulin fractions. Fig. 3 shows that prolonged column electrophoresis demonstrated the presence of both γ1 and γ2 labelled globulin.

Electrophoresis (fig. 4) showed that the specific activity of the albumin in the amniotic fluid was about 5 times that of the albumin in the fœtus, but apparently no other labelled protein was present in significant quantity. The amniotic fluid of the rhesus and green monkeys contained large amounts of a protein which moves on column and paper electrophoresis in the region of the α1 and α2 globulins; no peak of radioactivity was present in this position.

EXPERIMENTS ON ABSORPTION OF SERUM-PROTEINS FROM AMNIOTIC FLUID
(Monkeys E and F)

Procedure

Maternal serum-proteins prepared in the same way were injected percutaneously into the amniotic cavity, using a no. 23 gauge needle in the conscious animal, after mixing with 3 ml. of amniotic fluid removed previously through the same needle. Samples of the fluid were taken at operation 8 hours later (E), and at 3 hours and 6 hours (by aspiration through the abdominal wall and at operation 24 hours later (F). Cæsarean section was performed; samples of amniotic fluid uncontaminated with blood, and of maternal and fœtal blood, were taken; and the samples were fractionated.

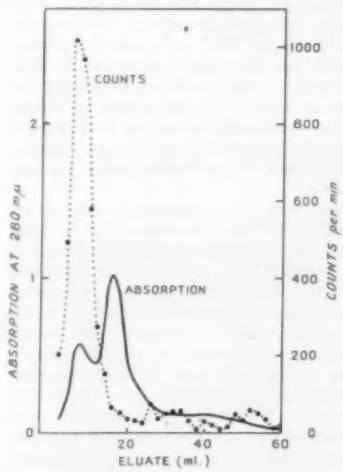

Fig. 4—Eluate of column electrophoresis of the concentrate of 4·0 ml. of liquor after treatment with deacidite FF (monkey D), 8 hours after the dose. The protein pattern shows a small amount of albumin and a large amount of another protein in the α1 and α2 globulin position. Labelled albumin is present but no other significant peak of radioactivity in the region of the globulins.

Results

The same total amount of activity was injected into the amniotic fluid (volume 100–120 ml.) as was injected intravenously in monkeys B, C, and D whose intravascular plasma volume was estimated to be about 250–300 ml. The specific activity of the albumin in the liquor of E and F obtained at 8 and 6 hours after injection was about 100 times greater than that present in the liquor at operation in monkeys B, C, and D. Fig. 5 shows that, after absorption of the iodide bound to albumin by passing through deacidite FF, only very small quantities of labelled proteins were present in the fœtal serum even after 24 hours. Electrophoresis of serum mixed with the contents of the duodenum and jejunum, and the ileum of the fœtus of E, showed an almost normal pattern of labelled serum-proteins present in fairly high concentration. The fœtus had therefore swallowed liquor and had the opportunity to absorb proteins from the gut, and at least some of all the major components of serum-proteins had escaped digestion. The maternal serum at operation 24 hours after the dose (F) contained small quantities of labelled albumin; assuming that it had equilibrated throughout the whole albumin pool of the mother, this labelled albumin would account for very roughly 0·1% of the dose albumin. Some of this might well represent some of the dose that had leaked out through the three needle tracks made through the fœtal membranes.

DISCUSSION

The validity of these experiments rests on the biological normality of the ^{131}I-labelled proteins.

There is now reasonable evidence that proteins iodinated with an average of 1 atom per molecule behave metabolically with close similarity to proteins labelled with ^{14}C-aminoacids, at any rate in rabbits.[8,9] If labelled proteins are allowed through the placenta, then one may fairly assume that unlabelled ones can also pass. Exact measurements of labelled proteins (albumin in particular) were difficult because of the tendency to adsorb free labelled iodide, which from trichloracetic acid (T.C.A.) precipitation studies was found to be present in relatively high concentration in fœtal serum and liquor, even in the presence of carrier. It is believed, however, that passing the serum through deacidite FF stripped most, if not all, of this adsorbed iodide.

The experiments demonstrate two main points. First, they show the direct transmission of homologous maternal albumin and γ-globulin to the fœtal circulation; this transfer is selective in that γ-globulin is transmitted some 15–20 times more easily than albumin. Globulins with a mobility in the α2 and β globulin region (in the conditions of electrophoresis used) do not appear to reach the fœtal circulation. This is in accord with the prediction based on studies on changes in protein-fraction concentrations in infants and children.[10] Selectivity of serum-protein transfer has been demonstrated (for homologous and heterologous serum-proteins [11] and for homologous and heterologous antibodies [12] by the endoderm of suckling rats. Selection of proteins in the rabbit is known to be controlled by the yolk-sac splanchnopleur, which is also entodermal.[1,13,14] The transplacental selectivity in the monkey thus appears to be one of the rare instances of selection by a non-entodermal surface. The selection of particular types of homologous antibody [15–20] illustrates how discriminating the human placenta can be.

Secondly, it has been shown that the transfer of the albumin and γ-globulin to the fœtus is not via the amniotic fluid but is presumably transplacental. In the late stages of pregnancy very little, if any, of the proteins was absorbed unchanged from the amniotic fluid. This was predicted for antibodies by Wasz-Höckert et al.[21] who found that in newborn infants with partial and complete œsophageal atresia the blood-level of diphtheria antitoxin was comparable with that of normal infants. The likelihood that proteins are absorbed from inhaled amniotic fluid also becomes remote.

The protein composition of the amniotic fluid of the rhesus monkey near term was, however, different from that of human amniotic fluid at term. The total protein concentration was about one-tenth that of serum; there was a small amount of albumin, and very small quantities of β and γ globulins. About 60% of the protein was of low

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molecular weight; and on electrophoresis, under the conditions used, it travelled between the $\alpha 1$ and $\alpha 2$ globulin. Whereas labelled albumin passes to the amniotic fluid from the maternal circulation, only very small quantities, if any, return to the mother. Since so little gets into the fœtus we infer that there is proteolysis within the amniotic cavity.

These points are under investigation, and a further report, with a quantitative analysis of the above experiments, will be given in due course.

SUMMARY

The transfer of ^{131}I-labelled serum-proteins from the maternal circulation to the fœtal circulation has been investigated in near-term pregnant rhesus monkeys.

The direct transfer of labelled $\gamma 1$ and $\gamma 2$ globulin has been demonstrated. Albumin is transmitted with much less relative facility, and little, if any, other globulin is transferred. Only labelled albumin was found in the amniotic fluid.

Labelled maternal serum-proteins injected into the liquor were not found in the fœtal circulation 24 hours later. Only extremely small quantities were found in the maternal circulation.

The transfer of γ globulin is thus shown to be transplacental in one species of primate, and the placenta is shown to be another rare example of a non-entodermal membrane capable of selective transmission of protein.

It is a pleasure to thank Dr. A. S. McFarlane and Mr. R. C. Holloway for assistance in preparing the labelled serum; Dr. K. Sykes and Dr. P. Frost for help with anæsthesia; and Dr. C. P. Farthing and Mr. W. E. Brocklehurst for help at operations; and Mr. D. Short and Dr. F. Hawking for assistance in obtaining the monkeys.

D. R. BANGHAM
M.B. Lond.
K. R. HOBBS
R. J. TERRY
PH.D. Leeds

National Institute for Medical Research, Mill Hill, London, N.W.7

Reviews of Books

The Kidney

An Outline of Normal and Abnormal Structure and Function

H. E. DE WARDENER, M.B.E., M.D., F.R.C.P., senior lecturer in medicine, St. Thomas's Hospital, London. London: J. & A. Churchill. 1958. Pp. 338. 45*s*.

THERE are a number of books on the kidney in which physiologists lay down canons of behaviour for the diseased kidney, or pathologists infer from their sections how the kidney must have behaved in life. Neither approach has been particularly helpful in the practical management of renal disease, whose study has on the whole progressed through the recognition of clinical syndromes which can be investigated and treated even when their precise ætiology may be a matter of surmise. Fuller Albright is reported to have said that we may soon know everything that matters about rheumatoid arthritis, except its cause and cure; a similar thrust could be made at our present clinical approach to renal disease, but a reading of Dr. de Wardener's book goes far towards rebutting it.

The background of physiology and the description of syndromes are clearly presented, with the authentic touch of the contributor to knowledge: and there is also a good, if brief, account of the contribution which renal biopsy and other techniques can make to ætiological diagnosis; a proper emphasis on the importance of the treatable disease, acute pyelonephritis; some indication of the complicated relationship between renal disease or dysfunction and hypertension, œdema, and extrarenal disease; and an adequate survey of available treatment.

The manner of presentation sometimes fails to equal the excellence of the matter. The sequence of short and unrelated chapters towards the end of the book is irritating, and some rearrangement might help the reader here; though a sentence like the penultimate one on p. 247 would defy interpretation in any context, unless perhaps A.C.T.H. is a misprint for A.D.H. or D.C.A. Most of the illustrations and charts are helpful; but those students with a perverse appetite for complexity will find satisfaction in figs. 36 or 37.

These criticisms must not obscure our view that this is a stimulating and valuable textbook, which should be read by all students of renal disease. We hope that Dr. de Wardener, having achieved a masterly synthesis of refractory material, may go on to excel himself in clarity in the second edition.

Leptospirosis in Man and Animals

J. M. ALSTON, M.D., F.R.C.P.E., Whittington Hospital, London.; J. C. BROOM, O.B.E., M.D., Wellcome Laboratories of Tropical Medicine, London. Edinburgh and London: E. & S. Livingstone. 1958. Pp. 367. 40*s*.

THERE is a lot to be said for the monograph. The textbook of medicine tells us only so much bacteriology as is useful in diagnosis; that of bacteriology lays more emphasis on morphology and systematics than on epidemiology. This monograph includes both and adds much more, and by its wider view allows us to make some reasonable guesses at the place in Nature of the genus Leptospira. For many years the authors have been recognised as the final court of appeal in their subject. Not only have they added much to knowledge but they have been liberal in their help and advice to others. They seem to have read everything which has been written in all civilised tongues and they are generous in their acknowledgment of the pioneer work of the others whose portraits add interest to their book.

It would be both pointless and ungrateful to search for omissions: a frustrated reader can be assured that a letter to the authors will obtain a speedy and helpful reply. The only suggestion which we would dare to make is that the future editions might benefit by the collaboration of a veterinary surgeon. By that time it may be easier to be dogmatic on the importance of the infecting strain of leptospira. We believe that in man *Leptospira icterohæmorrhagiæ* and *L. canicola* produce related but not identical ailments. Is there any virtue for the physician in distinguishing between infection with, say, *L. australis A* and *L. australis B*? Similar problems are obvious in other branches of bacteriology (for example, with staphylococci and salmonellæ) and the answers may have considerable effect upon the future of diagnostic bacteriology.

Psychiatry in the Modern World

E. B. STRAUSS, M.A., D.SC., D.M., F.R.C.P., lately physician in psychological medicine, St. Bartholomew's Hospital, London. London: Michael Joseph. 1958. Pp. 70. 8*s*. 6*d*.

IT has always been a pleasure to sit at the feet of Dr. Strauss, and his many disciples will not be disappointed with this little book. Drawing from his five recent articles in the *Sunday Times*, he discourses amiably about psychiatrists and psychologists, manic-depressives and schizophrenics, psychosomatics and somatotypes: always clear, always sensible, and often stimulating. The title may suggest a larger or more ambitious work, but the author himself admits he only touches on "the fringe of the fringe". It is a model of psychiatry made easy, however, and can be recommended to the lay public, to students, or to doctors who are looking for "an introduction to an introduction."

Especially commendable about the book is the author's neglect of sensation and his relative self-effacement: it is all too easy for the writers of such books to glorify the Ego with long accounts of interesting cases completely cured and invidious comparisons of the views of others with their own. Perhaps we should call a halt to these little books now, until there are some new advances for the public to be told about: it will in any case be hard to improve on the writing in this one. But why does Dr. Strauss think that "shock therapy" is an inappropriate name for E.C.T.?

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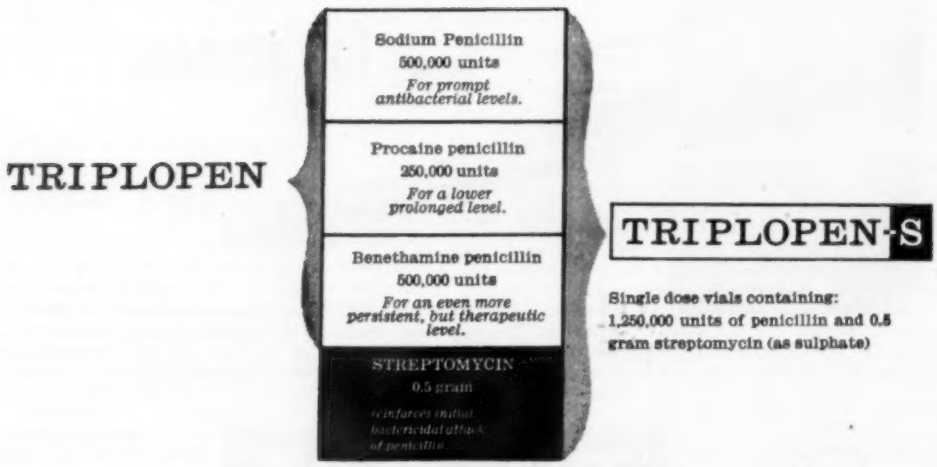

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Effects of Radiation

SINCE the Medical Research Council's committee on radiation hazards made its report [1] in June, 1956, many new data on the biological effects of ionising radiations have been assembled; but the United Nations report,[2] made known on Sunday, shows that more than two years of intense study and analysis have not elicited answers to some disturbing questions. The doubt remaining at the root of all disquiet is whether or not there is a threshold at which radiation damage begins and below which no harm results. The United Nations committee (whose report is described on p. 360) cannot answer this question (indeed, it is doubtful whether it will be answered in the near future). So the fears we expressed [3] two years ago, and to which we have returned from time to time, remain unrelieved.

The genetic damage which additional radiation may induce and which may be manifest in later generations has been in the forefront of discussion. The medical applications of radiation are here the greatest hazard—in countries where such applications are common. The M.R.C. report estimated that diagnostic radiology in Britain contributed a population gonad dose of at least 22% of natural background radiation; and the United Nations committee confirm the " at least " when they say that the values put before them for the genetically significant doses from medical procedures are " of the same order " as the doses from natural sources. Background radiation supplies an estimated genetically significant dose of 3 rem in thirty years; and man-made sources (excluding environmental contamination and occupational exposure) are put in the range 0·5–5 rem. For this total, diagnostic X-ray examinations are largely responsible, and 80–90% of the diagnostic dose to the gonads comes from a few types of abdominal and pelvic examination. The reinforced lesson in these new estimates is that greater efforts must be made to restrict the gonad dose in medical irradiation, and stricter judgment must be used before patients are exposed to the crucial pelvic and abdominal investigations. Detailed inquiries into doses administered in radiological practice are in hand in this country and elsewhere; but there is no need to wait for more facts before renewing the advice of the M.R.C. committee that " the time has come for a review of present practice in diagnostic radiology ". What has been made known in the past two or three years has already prompted caution in the medical use of radiation: alarms should not be so vivid that valuable information is left unsought when it may be of vital concern to the patient, but the words of the U.N. report must now add a new warning: " Medical and industrial procedures tending to increase radiation levels to which human populations are exposed should be carefully weighed as to such benefits or hazards as they may have."

Radiation-induced mutations are in general harmful, and increase in direct proportion to the genetically significant exposure, even at very low doses; and this accepted qualification must temper the apparent reassurance provided by the committee's figures for the genetic effect of environmental contamination by radioactive substances released in the testing of nuclear weapons. If weapon tests cease this year the thirty-year " genetic " dose is put at 0·010 rem (which agrees with the M.R.C. committee's view of " less than 1% of natural background "). If tests continue according to either of the two assumptions set out on p. 361, this dose may increase to 0·06 or 0·12 rem (2% or 4% of background). From these and many other figures before them the U.N. committee assess (" with wide margins of uncertainty ", particularly about the dose required to double the mutation-rate) that a situation of fallout equilibrium, reached after long-continued testing, may be associated with from 500 to 40,000 annual instances of major genetic defect, compared with an estimated natural occurrence of 700,000 to 3 million yearly among a future world population of 5000 million. The existing and expected " normal " burden of genetic defect is enormous: the estimated addition by fallout is slight; but it is nevertheless an addition.

When they come to put a value on the somatic risk, on what may happen to those now living as a consequence of man-made contamination of the environment, the U.N. committee are more perturbing. People who derive most of their dietary calcium from rice and vegetables may experience a mean marrow dose of 7·5 or 17 rem over seventy years if weapon tests continue to equilibrium under one or other of the committee's assumptions. In the same period natural sources give an estimated marrow dose of 7 rem. Even if weapon tests stop this year, a seventy-year marrow dose of 0·96 rem is possible from fallout products. This is a dose equivalent to slightly more than that delivered by 10 strontium units; and the M.R.C. report said that " immediate consideration would be required " if the concentration of radioactive strontium in human bones showed signs of rising greatly beyond 10 strontium units. For milk-drinking, rather than rice-eating, peoples the outlook is better. At the highest estimate the marrow dose from fallout products will be 2·8 rem. in seventy years, and if tests stop now the dose may be limited to 0·16 rem. These figures, however, can be given very different meanings while nothing certain is known about thresholds. Thus, on the assumption that there is no threshold for leukæmia the U.N. report estimates that

1. Hazards to Man of Nuclear and Allied Radiations. Cmd. 9780. H.M. Stationery Office.
2. Report of the United Nations Scientific Committee on the Effects of Atomic Radiation. New York, 1958. Obtainable from H.M. Stationery Office, P.O. Box 569, London, S.E.1. Pp. 228. 18s.
3. *Lancet*, 1956, i, 999.

equilibrium fallout may eventually mean 5000 to 60,000 cases of leukæmia a year. But if a threshold is put at 400 rem it is unlikely that there will be any additional leukæmia. If there is no threshold and tests stop soon, 400–2000 leukæmias a year may temporarily result; if 400 rem is the key level, nothing. Even though these estimates are admittedly very uncertain, they must be respected for the long and careful judgment that backs them. They are a warning of what *may* happen if the release of radioactive poisons is allowed to continue.

As an agreed international statement of opinion based on as wide a survey as possible, the U.N. document is a notable achievement. Its confirmation of so many of the findings of the M.R.C. committee, pronounced more than two years ago, is a striking tribute to that committee.

Fertility and Mental Illness

THE extent to which people liable to mental affliction procreate has long concerned those administering mental-health policy. Between the wars large families among the lower social classes led to fears (now largely dissipated) about declining national intelligence and to the closely related fear that unrestricted breeding among stock of poor mental background was creating an increasing problem of mental disorder. Beliefs have sprung up with the most far-reaching effects: sterilisation schemes—voluntary, pseudo-voluntary, and compulsory—have been advocated. Prof. GLANVILLE WILLIAMS [1] has given us the most up-to-date and comprehensive survey of the approaches to sterilisation here and in America and argues persuasively for legalisation and wider use, although some of his grounds must remain open to question. The importance of these issues and the power with which views on them are expressed make it appropriate that Prof. AUBREY LEWIS should have examined in detail some of the evidence. His critical survey of work on the fertility of the mentally ill (but not of the mentally defective) in a Galton lecture [2] shows how few and contradictory are the facts so far obtained.

He pointed out that a hundred years ago the concept of "degeneracy" was put forward by MOREL,[3] and until the turn of the century it was thought that inferior stock underwent decay generation by generation, psychopathy breeding neuroses, then at a younger age schizophrenia (the origin of the term "dementia præcox"), the line being extinguished when idiocy in childhood precluded further procreation. Such a tidy scheme fitted in well with current religious beliefs on reprobation and the sins of the forefathers being visited on the children, and with LOMBROSO's views on atavism and criminal types. HENRY MAUDSLEY [4] in 1862 subscribed to it, and even ADOLF MEYER agreed. But in the early 1900s the pendulum swung to the other extreme, and DAVID HERON [5] in 1907 expressed the belief that marriages of the insane were *more* fertile than others. The idea of Nature's beneficent hand extinguishing its less useful members was now replaced by a fear of unrestricted proliferation among the mentally diseased. Despite the exposure of fallacies in method and reasoning, the belief persisted, and it was not until the 1930s that the matter was really put to the test. DAHLBERG [6] in Sweden and DAYTON [7] in the U.S.A. showed independently that the pre-admission fertility of insane married women was significantly *lower* than among a comparable group of women in the general population. It remained for Professor ESSEN-MÖLLER [8] in Sweden to compare the two main diagnostic categories—manic-depressives and schizophrenics. From a group of nearly 5000 married patients he deduced that manic-depressives were about as fertile as the general population. The schizophrenics, on the other hand, were as a whole about a quarter as fertile as the general population; but more detailed analysis showed that schizophrenic men before their illness had average fertility, whereas women were about half as fertile as normals. Over the years both sexes followed the national decline in birth-rate more slowly than was expected, until the pre-schizophrenic women were about as fertile as normals. After the onset of the illness the birth-rates, as expected, fell greatly. Patients who married after the illness (presumably mild) had developed were normally fertile. Paradoxically the birth-rate was higher than expected in the year before admission. On close examination this seemed to be a sociopsychological phenomenon due to postponement of admission until after the birth. More recently BÖÖK,[9] surveying a shut-off community in North Sweden, found that the fertility of marriages contracted by schizophrenics was very slightly *greater* than normal; but fertility of the unmarried schizophrenics was lower than among others, and as 75% of the men were single the over-all fertility was well below that of the normal population. It appeared, therefore, that lowered fertility among schizophrenics might be an index of the lower chances of marriage rather than an effect of the disease itself. The preponderance of single persons over married among schizophrenics has often been noted; NORRIS,[10] for example, found in English male patients about six times as many unmarried as married on first admissions. The most probable reason seemed to be that the premorbid "schizoid" personality makes marriage less likely, although the protective effect of an affectionate home life and enhanced likelihood of being sent to hospital may play a part. A man who is shy and indrawn is at a special disadvantage in our culture; whereas a woman of this type is more likely, perhaps, to contract matrimony. It is evident, though, from BÖÖK's figures that the probabilities vary in different environments: his schizophrenic women had a much better chance of marriage than those of other communities studied.

1. The Sanctity of Life and the Criminal Law. London, 1958.
2. *Eugen. Rev.* 1958, **50**, 91.
3. Morel, B. A. Traité des dégénérescences physiques, intellectuelles, et morales de l'espèce humaine. Paris, 1857.
4. *J. ment. Sci.* 1862, **8**, 61.
5. A First Study of the Statistics of Insanity and the Inheritance of the Insane Diathesis. London, 1907.
6. Dahlberg, G. *Z. ges. Neurol. Psychiat.* 1933, **144**, 427.
7. Dayton, N. A. *Stud. quant. cult. Sociol.* 1930, **24**, 123. New Facts on Mental Disorders. Springfield, Ill., 1940.
8. Essen-Möller, E. *Acta psychiat., Kbh.* 1935, suppl. 8. *Arch. Rass.- u. GesBiol.* 1936, **30**, 367.
9. Böök, J. A. *Acta genet.* 1953, **4**, 133.
10. Norris, V. A. *J. ment. sci.* 1956, **102**, 467.

Having concluded that the fertility of schizophrenics was low, Professor LEWIS considered the possible factors maintaining the disease at its present level: he subscribed to the view that spontaneous gene mutation occurs at a high rate, and he called attention to the Medical Research Council report on the possible effects of radiation.[11] Mental illness, it said, is the most important single category of disease determined largely by heredity, and he believed that increased radiation may be raising the mutation-rates for these diseases.

The fertility of neurotic persons is almost completely unknown. One study [12] suggested a vague link between small families and feelings of inadequacy in the parents, but unpublished work at the Maudsley Hospital on a limited sample has shown no differences in fertility or in the number of single women. The psychological mechanisms believed to play a part in sterility, and the sexual disturbances which so often plague the neurotic, may be expected to affect birth-rate, but so far nothing has been proved.

Professor LEWIS speculated on the possible consequences of present mental-hygiene campaigns, which, very laudably, seek to instil into the public a more sympathetic and informed understanding of mental illness. To play down the differences between mental and physical illness, and to ignore the genetic implications, might, he suggested, lead to higher marriage-rates among those liable to manic-depressive illness or with a schizoid personality: a contributory factor might be the increasing use of treatment in the community and shorter periods in hospital. With increased birth-rates among these groups there would be more children destined to become mentally ill, and such children would be in the care of parents liable to spend periods in mental hospitals—a thing which he felt no humanitarian person could regard with equanimity. On this most important subject we agree with Professor LEWIS that hereditary factors should be squarely faced both by ourselves and by the public, and that the risks of marriage and procreation should be made known as fairly as possible in the light of present knowledge: this is already the standard practice in the case of epilepsy, where commonly the normal marriage partner undergoes electroencephalographic examination in order that the chances of epilepsy in the children may be assessed. While no-one would wish to ignore the effects of environment in the formative years of life, the psychodynamic view of causation must not be allowed to obscure the work of KALLMANN [13] and others on heredity. No person must be deprived, against his will, of the fundamental right to procreate (especially at our primitive level of knowledge); but we as doctors would be doing less than our duty if we did not place the facts, as far as they are known, before our patients and the public. Further work is badly needed, and no-one is better placed than Professor LEWIS to see that it is properly carried out.

11. Hazards to Man of Nuclear and Allied Radiations. H.M. Stationery Office, 1956.
12. Westoff, C. F., Kiser, C. V. *Millbank Mem. Fund Quart.* 1952, **30**, 239.
13. Kallmann, F. J. Heredity in Health and Disease. New York, 1953.

The Anatomy of the Cardia

FOR some time investigation of the lower œsophagus was out of phase, for diseases in this region were well documented while anatomical study lagged behind. In hypotheses about the mechanism of closure at the cardia, extrinsic pinchcocks replaced intrinsic valves, while deviationists concerned themselves with the acuteness of the angle between œsophagus and stomach. Recently, however, intrinsic valvular mechanisms have returned to favour. By marking the anterior edge of the diaphragmatic hiatus at operation with a clip, BOTHA showed that the manner in which the crura embrace the œsophagus at the hiatus can have little effect on the closure mechanism; for when the diaphragm contracts the gastric fundus is pushed downwards in relation to the hiatus,[1] thus opening the gastro-œsophageal angle and vitiating any sling effect the crura might have at that point. Radiographically controlled studies undertaken by him with ASTLEY and CARRÉ [2] pointed to the lower œsophagus as an area which, in the majority of the 18 persons investigated, provided a pressure "barrier" between stomach and upper œsophagus; this lay above the level of the hiatus. ATKINSON et al.[3] confirmed this finding; they showed that the pressure differentials were removed by swallowing, and that in cases of reflux the pressure barrier was absent. That the barrier in no way relies on the diaphragm for its existence they proved conclusively by demonstrating its presence in a case of hiatus hernia without reflux when the barrier was quite definitely above hiatal level. In a converse fashion they found that the barrier was eliminated in a case subjected to Heller's operation when particular care had been taken not to damage the hiatus. From their radiographic studies they were likewise unable to demonstrate any correlation between reflux and angle of entry of the œsophagus into the gastric hernia in cases of hiatus defect. The recent findings thus suggest that a sphincter exists, if not in the palpable anatomical sense, certainly in the all-important functional sense; and in this respect JOHNSTONE's [4] report of a woman who suffered œsophageal reflux only when tired is of interest. The understanding of reflux has now a firmer basis; and treatment of œsophagitis, particularly as regards surgical technique, can be designed more rationally.

BOTHA [5] has now added to knowledge of the gastro-œsophageal junction by showing that many people have mucosal folds which, when drawn together, act as a cork to close the top of the stomach. These folds are not valvular and mechanical but are thrown up longitudinally by contraction of muscularis mucosæ. The presence of such folds has been in doubt since MAGENDIE first described them; indeed BOTHA's work left him in doubt until he began to study the living organism instead of specimens. (The pathological condition of lower œsophageal ring appears to be due to hypertrophy of the

1. Botha, G. S. M. *Lancet*, 1957, i, 662.
2. Botha, G. S. M., Astley, R., Carré, I. J. *ibid.* p. 659.
3. Atkinson, M., Edwards, D. A. W., Honour A. J., Rowlands, E. N. *ibid.* 1957, ii, 1138.
4. Johnstone, A. S. *Brit. J. Radiol.* 1955, **28**, 2.
5. Botha, G. S. M. *Brit. J. Surg.* 1958, **45**, 569.

muscularis mucosæ at this site [6]; but the outcome is a horizontal shelf.) It should occasion no surprise that several factors combine to ensure closure of the cardia, for most physiological mechanisms are complex; BOTHA hints that the relative importance of each factor varies from one person to another.

There is need for further anatomical study to establish whether or not columnar epithelium in the lower œsophagus is a variant of normal; BARRETT [7] regards its presence there as abnormal and speaks of those with this condition as patients, even though they may be symptom-free; ALLISON and JOHNSTONE [8] presumed that the presence of gastric mucosa of cardiac type in the œsophagus may be a congenital abnormality. Yet BOTHA finds that the junction of squamous and glandular epithelium is above the cardia in most people. Does it really matter? The discussion which this "ectopic" epithelium has provoked seems to be out of proportion to its probable importance. A full study of this histological point should give a firm statistical answer which might remove one distraction in arguments on the causation of peptic ulcer of the œsophagus. And if anyone has difficulty in differentiating œsophagus from stomach (as BARRETT [7] points out, the presence of mucosa is the usual indicator) then the pressure barrier might aid in defining the lower limits of œsophagus.

Annotations

B.C.G. IN THE U.S.A.

A LARGE trial of B.C.G. vaccination in the U.S.A. has been described by Palmer et al.[9] This took place in two localities—Puerto Rico and two counties in Georgia and Alabama. The groups studied differed considerably and were apparently subject to different risks of tuberculosis; they are therefore considered separately. The Puerto Rican population consisted of children and adolescents under 19 years of age; whereas the population studied in Muscogee and Russell counties contained people of all ages, more than half being over 19 and almost a fifth 40 years old or more. Among the 191,827 young Puerto Ricans there were about 40% "positive" to a 10 T.U. Mantoux test; among the 16,125 under 20 in Muscogee and Russell only 14% were "positive" to a 5 T.U. test. The tuberculin-negative individuals in both trials were divided into vaccinated and unvaccinated groups. The morbidity experience of the three groups—initially infected, vaccinated, and unvaccinated—was compared over periods of six to seven years. The measure of morbidity was obtained from the number of cases of tuberculosis known to have arisen within these groups through the existing medical, public-health, and vital statistics reporting systems in the two localities; the people in the trials were not individually followed up and examined.

Although this method may enable valid comparisons to be made within the two populations studied, it does not permit accurate comparison between them or with other similar trials. In Puerto Rico the average annual incidence per 100,000 was 163 among the initially infected, 43 among the initially uninfected and unvaccinated, and 30 among the vaccinated. 856 (75%) of the 1149 reported cases of tuberculosis occurred in those found to be infected at the time they entered the trial. In Muscogee and Russell the corresponding rates were 78, 22, and 14; and 161 (75%) of the 216 reported cases were in those already infected. It was concluded that the reduction of tuberculosis attributed to vaccination was 31% in Puerto Rico and 36% in the Georgian and Alabama districts among those not already infected when the trial began. If all the uninfected in the Puerto Rican group had been vaccinated there would have been a 7·9% reduction in known tuberculous morbidity in the whole population studied in the period of six to seven years, and a 9·3% reduction in Muscogee and Russell counties.

The findings are compared with those of the rather more precise trial carried out by the Medical Research Council.[10] In this, the estimated reduction in morbidity that could have been obtained (assessed by individual follow-up) over a period of two and a half years in the initially uninfected was reported to be 82%, compared with the reduction of only about 30% in the American trial. These and other differences between the trials are discussed in the report, and it is concluded that the apparent differences in the effectiveness of B.C.G. vaccination are inexplicable. But the two trials are not comparable in many respects—in particular, the ages of the subjects. The British trial concerned only children aged 14–15, adolescents approaching the time of leaving school. The efficacy of vaccination among these may not be the same as among infants, young children, or adults, even of the same race and in the same environment.

Palmer et al. conclude that extensive vaccination is not indicated in the United States. They state that "because B.C.G. cannot help those who are already infected, nor those who will not become infected, and may be helpful only to a portion of the decreasing few who will become infected in the future, it is apparent that vaccination cannot be very useful in controlling tuberculosis in this country". Presumably this is meant to apply to all large-scale vaccination of groups of people, whether defined by age or by special risk of exposure to infection (such as nurses, medical students, laboratory workers, and the families of known tuberculous patients). The assertion loses some of its force by containing such an indefinite attribute as "very useful". To gain even a 30% chance of preventing tuberculous illness in a baby exposed to an infectious mother might be thought very useful by the parents; and to prevent one person within each affected household from becoming ill could be considered a very useful contribution to controlling tuberculosis within the community.

Whether widespread and expensive public-health endeavours to vaccinate large numbers of people is justified can be determined only by taking into account epidemiological, economic, and political factors unknown to those who are not intimately acquainted with that community. A recommendation to limit or avoid using B.C.G. vaccination as a centrally controlled public-health measure may well be right in a particular situation. But such a recommendation does not condemn vaccination in all other situations—as is clearly recognised by Palmer et al.—or in individual cases. A measure may not be very

6. MacMahon, H. E., Schatzki, R., Gary, J. E. *New Engl. J. Med.* 1958, **259**, 1.
7. Barrett, N. R. *Surgery*, 1957, **41**, 881.
8. Allison, P. R., Johnstone, A. S. *Thorax*, 1953, **8**, 87.
9. Palmer, C. E., Shaw, L. W., Camstock, G. W. *Amer. Rev. Tuberc.* 1958, **77**, 877.
10. Medical Research Council. *Brit. med. J.* 1956, i, 413.

useful for maintaining the health of the public; but it may be invaluable for preventing an individual dying. The committee on therapy of the American Trudeau Society has just issued a statement on the role of B.C.G.[11] It states that B.C.G. has a place in preventing tuberculosis and suggests certain groups in which it might profitably be used. These are almost the same as the groups now being vaccinated in Great Britain, with the exception of the adolescent children throughout the country, the committee including only children living in areas with a high prevalence of tuberculosis. The statement concludes: "It is the responsibility of the physician to weigh the advantages and disadvantages in a particular situation."

SPREAD OF STREPTOCOCCI

THREE months ago [12] we drew attention to a current study by Holmes and Williams [13] of streptococcal infections and their probable sources among a large population of children in a residential Dr. Barnado's Home over a period of $3^1/_2$ years. The reduction of so large a mass of epidemiological data to a useful form is no easy matter; Holmes and Williams have ordered their material so as to provide maximum information with maximum clarity in a way which deserves much admiration. In their concluding chapters [14] they have attempted not only to assess the factors influencing individual susceptibility to streptococcal infection under institutional conditions but also to analyse the many differing effects which the organism, the host-carrier, the environment, and the method of treatment may have on the epidemic pattern in such a community.

In the matter of susceptibility, the pros and cons of tonsillectomy have been much discussed. Holmes and Williams' analysis shows that their tonsillectomised children individually derived moderate benefit, in that subsequently they suffered from few streptococcal sore throats. The effect of tonsillectomy, however, seemed to be less in protecting the children's throats against colonisation by streptococci than in preventing clinical illness accompanying infection. A potential social disadvantage which may follow tonsillectomy is the high nasal carriage-rate of streptococci during or after streptococcal throat infection; and Holmes and Williams find some indication that the non-type-specific immunity which follows exposure to group-A streptococci (whose existence was strongly corroborated by this study) may be impaired when tonsils have been removed. Moreover, type-specific immunity was found to be a significant factor in protection against reinfection under communal conditions, affording considerable protection on re-exposure to the homologous type. Some evidence, too, was obtained that type-specific immunity was evoked by exposure without frank clinical infection.

Analysis of spread of infection within the subcommunities studied showed the importance of the introduction of new types of group-A streptococci. Reinfection on re-exposure to a given type was rare. Consecutive large epidemics were never due to the same type, and where there had been an epidemic due to one type the number of cases observed at a subsequent introduction was roughly inversely proportional to the number in the original outbreak. Whether certain types of group-A streptococci are more communicable than others remains undecided. It may be significant that the prevalent types showed a rather greater frequency of nasal carriage among both cases and carriers.

"Dangerous carriers" are those with heavy nasal infection [15] and Holmes and Williams confirm this. In the groups of children studied, the presence of nasal carriers (whether in the incubating stage or convalescent) and the arrival of new children in the community combined to cause continued spread of infection within it. The fact that tonsillectomised children provided the majority of such dangerous carriers suggests that tonsillectomy has no place in controlling the spread of streptococcal infection. A much more effective measure is the eradication of streptococci from the throat by adequate penicillin treatment [16] (convalescent carriers were responsible for at least 25% of the secondary cases noted in this study). Much less important are environmental control measures: bedding and air disinfection play little part in disseminating streptococci.

The detailed analysis to which Holmes and Williams have submitted their data provides many valuable conclusions. The underlying lesson, perhaps, is that transmission of streptococcal infections is a matter of direct spread from infected individual to individual. The most effective transmitter is a person incubating an infection; it probably takes a healthy or convalescent carrier longer to transmit as much.

MIDGET ANÆSTHETIC MACHINES

NITROUS oxide is still the anæsthetic most commonly used for outpatients, but sometimes a more potent inhalational agent is valuable. Cyclopropane has been recommended for this purpose,[17] and two highly portable apparatuses have been developed to enable a few minutes of surgical anæsthesia to be produced with this agent.

One apparatus, developed in the United States,[18 19] delivers 40% cyclopropane with 30% oxygen and 30% helium. It incorporates a very small carbon-dioxide absorption canister of about 100 c.cm. capacity; accordingly a closed system of anæsthesia can be obtained for 3–20 minutes. This machine is also adaptable for resuscitation with 100% oxygen. The other apparatus, of English origin,[20] is more simply designed to give about $1^1/_2$ minutes' anæsthesia without carbon-dioxide absorption from a mixture of 50% cyclopropane, 25% oxygen, and 25% nitrogen. The gases for both machines are compressed in tiny disposable cylinders. Helium or nitrogen is necessary to render the mixture non-ignitable.

Such simple machines have several advantages: they are extremely portable, and they deliver a fixed concentration of gases that is known to produce good, though brief, surgical anæsthesia without hypoxia. The safety of a single dose of a high concentration of cyclopropane can reasonably be regarded as established by the many patients who have now been satisfactorily dealt with in this way without major complications.[19 21 22]

The title of Sir JOHN STOPFORD has been gazetted as BARON STOPFORD OF FALLOWFIELD, of Hindley Green in the County Palatinate of Lancaster. Dr. STEPHEN TAYLOR becomes BARON TAYLOR, of Harlow, in the County of Essex.

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Special Articles

EFFECTS OF ATOMIC RADIATION

United Nations Report

THE United Nations Scientific Committee on the Effects of Atomic Radiation was charged by the General Assembly with the task of studying and assessing observations supplied by member states on the levels of ionising radiation and radioactivity in man's environment and their effect upon him. The committee was established in December, 1955, and the report published this week records the results of a long and intensive study of a mass of information collected from all over the world. The text of the report is brief: far longer are the detailed annexes which summarise and analyse the technical data submitted to the committee. The report represents the most complete picture of the situation yet assembled, and we publish here some extracts from it.

The States represented on the committee were Argentina, Australia, Belgium, Brazil, Canada, Czechoslovakia, Egypt (later the United Arab Republic), France, India, Japan, Mexico, Sweden, U.S.S.R., the United Kingdom, and the United States. The United Kingdom was represented at the committee's first session by Prof. W. V. Mayneord and at subsequent sessions by Dr. E. E. Pochin.

LEVELS OF RADIATION

The committee has estimated the average amounts of radiation likely to be received by populations during specified periods. An averaging period of 30 years has been used as relevant to transmissible genetic changes and 70 years as far as somatic injury during the lifetime of an individual is concerned. Estimates for medical examinations and occupational exposures were based upon " the present situation in certain countries with developed facilities, rather than on a forecasted world average ".

Natural Sources

In certain parts of the world the natural background radiation dose may be as much as ten times greater than the worldwide average and the report points to the relevance of inquiries into the health of people living in such parts in expanding knowledge of chronic low-dose irradiation. Harmful effects attributable to radiation from natural sources are not known with any certainty, but, the report adds, it seems likely that some genetic, and possibly some somatic, injury is caused in this way.

Medical Procedures

In countries with extensive medical services, the radiation given for medical purposes makes the largest artificial contribution to the irradiation of the population, but no data are available for countries less fully provided with medical resources. The reported values of genetically significant doses are of the same order as the doses from natural sources. The contribution from diagnostic X-ray examinations greatly exceeds that from radiotherapy and radioisotope applications, and 80–90% of the total diagnostic dose to the gonads is due to relatively few types of examination of the abdomen and pelvis.

The significant dose to bone and bone-marrow from medical procedures has been less closely studied than the genetically significant dose, although it may be of importance if bone tumours or leukæmia are induced by low doses of radiation. Although individual marrow exposures vary very widely, the average is unlikely to differ greatly from that received by the marrow from all natural sources.

Occupational Exposure

Even in countries where occupational exposure is probably greatest it is estimated to contribute to the total irradiation of the population a dose of only about 2% of that from natural sources. But, the report goes on, with an increasing use of nuclear reactors and radioactive materials and probably of medical and industrial radiological procedures " this is clearly a figure which should be kept under close review ".

Fallout

The committee's estimates for the genetically significant and mean marrow doses from stratospheric fallout of nuclear-test material have been computed from worldwide average deposits. The radiation due to stratospheric fallout from weapons exploded so far will contribute, it is estimated, a 30-year gonad dose of 0·010 rem [1] and a 70-year per-capita mean marrow dose of 0·16 rem and 0·96 rem for two populations deriving most of their dietary calcium from milk and rice respectively. The corresponding estimated doses from natural sources are shown in the accompanying table. For 70-year mean marrow doses, a conversion factor of 14 turns rems into strontium units.[2]

Cæsium 137 (^{137}Cs) is responsible for most of the gonad radiation from fallout. It becomes distributed more or less evenly throughout the tissues, causing uniform irradiation of the whole body; and when present in the surroundings, its penetrating α-radiation causes a similarly uniform irradiation of tissues.

Strontium 90 (^{90}Sr) is not a gamma-emitter and does not contribute significantly to the irradiation of any part of the body from without, but its selective concentration in bone raises problems that do not appear with ^{137}Cs. The highest concentrations of ^{90}Sr in bone have been observed in children from a few months to five years old. The bone-marrow exposures from fallout shown in the table are due to the ^{90}Sr content of bone and refer to the concentrations estimated for children of these ages.

The ^{90}Sr concentration in bone is also affected by dietary habits and agricultural conditions and by the ratio of the amounts of ^{90}Sr to calcium in the diet; and the committee has assembled much useful data on these points. The estimates for bone-marrow exposures due to fallout are given for different conditions: one based on observations in the United States and the United Kingdom, where milk is the main source of dietary calcium and ^{90}Sr, and where soil calcium contents are commonly high; and the other based on data from Japan where milk products are much less used and where rice and other vegetable products form the main source of dietary calcium and ^{90}Sr and where low calcium soils are common.

It is evident, the report sums up, that the exposures from fallout which are most likely to be of significance are:

(*a*) Those from short-lived fission products and radioactive material from local or tropospheric fallout.

(*b*) Those of the gonads and other organs from ^{137}Cs due to stratospheric fallout.

(*c*) Those of bone and adjacent tissue from ^{90}Sr which also comes largely from the stratosphere.

BIOLOGICAL EFFECTS OF RADIATION

Present uncertainty about the effects of low dose levels makes it imperative, the report declares, that as much relevant information as possible be collected about groups of persons chronically exposed at these levels and

1. Dose in rem = dose in rad × relative biological effectiveness (R.B.E.). R.B.E. = 1 for X, γ, and β rays and 10 for α rays.
2. 1 strontium unit = 1 micromicrocurie of ^{90}Sr per g. of calcium.

ESTIMATED DOSE FROM DIFFERENT RADIOACTIVE SOURCES

Sources	Genetically significant dose (rem) (Maximum for any 30-year period)		Per capita mean marrow dose (rem) (Maximum for any 70-year period)			
Natural sources	3		7			
Man-made sources (except environmental contamination and occupational exposure)	0·5–5		Ranges beyond 7			
Occupational exposure	Less than 0·06		0·1–0·2			
			Estimates for countries deriving most of dietary calcium from milk		Estimates for countries deriving most of dietary calcium from rice	
Environmental contamination (hypothetical cases):						
Weapon tests cease at end of 1958	0·010		0·16		0·96	
	Assumption *a*	Assumption *b*	Assumption *a*	Assumption *b*	Assumption *a*	Assumption *b*
Weapon tests continue until equilibrium is reached in about a hundred years	0·060	0·12	1·3	2·8	7·5	17

Assumption *a* is that the injection-rate of radioactive material is such as to maintain a constant fallout-rate of ^{90}Sr and ^{137}Cs. Assumption *b* is that weapon tests equivalent in release and stratospheric injection of fission products to the whole sequence of weapon tests from the beginning of 1954 to the end of 1958 will be repeated at constant rate.

for whom adequate control groups exist—for instance, certain populations in areas of high natural radiation and workers in uranium mines. A W.H.O. expert committee has recently been planning such an inquiry, and they have in mind the monazite region of Kerala in India.

Genetic Effects

Exposure of gonads to even the smallest doses of ionising radiations can give rise to mutant genes which accumulate, are transmissible to the progeny, and are considered to be, in general, harmful to the human race. A dose of between 10 and 100 rads per generation would probably be required to double the natural mutation-rate in human populations. Besides increasing the incidence of easily discernible disorders, increased mutation may affect certain universal and important "biometrical" characters, such as intelligence and life-span. Continued small genetically significant exposure of a population may affect not only a correspondingly small number of individuals seriously but also most of its members to a correspondingly small extent. From the genetic facts it studied the committee concluded that exposures to ionising radiation should be reduced wherever possible, and that medical and industrial procedures tending to increase radiation levels to which human populations might be exposed should be carefully weighed as to such benefits or hazards as each may have.

Threshold or No Threshold?

The dose-effect relationship may be of two general types: the effect may be directly proportional to the dose; or there may be a threshold below which no effect occurs. Intermediate relations may be assumed to exist, represented by a curved line, showing extremely little effect at low dose, thus indicating an "apparent" threshold. All studies of the dose-effect relationship are complicated by the unavoidable presence of natural radiations. In man the annual dose from natural radiations is about 100 millirem. It is assumed that a certain amount of genetic damage in man is caused by these radiations: it is conceivable that analogous changes may occur in somatic cells and that such changes, being cumulative with age, may have adverse influences. But there is at present no evidence for such an assumption.

In human adults it is difficult to detect the effect of a single exposure to less than 25 rem, or of continuing exposure to levels below 100 times the natural. Morphologically recognisable damage may be induced by total or partial, continuous or intermittent irradiations much in excess of the currently accepted "maximum permissible levels" of occupational exposure—such damage as leucopenia, anæmia, and leukæmia. As the dose of radiation is reduced below the amounts giving rise to acute functional or morphological alterations, the reactions of the organism become more difficult to detect immediately and the effects may be progressively delayed in time. Thresholds are not easily revealed under these conditions of exposure; in fact, for some of the most delayed phenomena, the report adds, it is uncertain whether they exist. "At the present time, due to the fact that threshold doses for the delayed somatic effects of radiation are not exactly known, it must be recognised that the exposure of human populations to increasing levels of ionising radiations may cause considerable and widespread somatic damage."

ESTIMATES OF CONSEQUENCES

The report emphasises that any attempt to evaluate the effects of sources of radiation to which the world population is exposed can produce only tentative estimates with wide margins of uncertainty. Nevertheless, on the basis of the dose estimates and the available data about likely somatic and genetic effects of given exposures, the committee have tried to evaluate the possible effect of natural and fallout radiation in causing leukæmia and major genetic effects. These estimates indicate only the order of magnitude of the frequency with which effects may be produced, and "our ignorance as to whether thresholds exist . . . cause the greatest uncertainty in the estimates".

Leukæmia

The natural incidence per year in the present world population is put at 150,000, of which 15,000 is attributable to natural radiation. *If there is no threshold* and weapon tests stop this year, fallout radiation may produce an estimated 400 to 2000 cases of leukæmia annually, up to an estimated eventual total of from less than 25,000 to 150,000 cases. *If there is no threshold* and fallout is allowed to reach equilibrium after prolonged continuation of tests, the leukæmia-rate due to fallout may be 5000 to 60,000 cases per year (compared with a natural incidence of 250,000, the world population being assumed to have increased from 3000 million to 5000 million). In another series of calculations the committee assumed a threshold of 400 rem. Under these circumstances the estimates for fallout leukæmia drop to zero, unless individual bone-marrow dose exceeds the mean value by a large factor.

Major Genetic Defects

Assuming a future world population of 5000 million, the natural *annual* occurrence of major genetic defects is put

in the range 700,000 to 3 million cases. Of this total, natural radiation may account for 25,000 to 1 million. If tests stop in 1958, a total of 2500 to 100,000 cases may arise over subsequent years as the result of genetic damage due to fallout radiation. If tests go on to equilibrium the estimate for fallout-determined genetic defects is 500 to 40,000 cases per year.

CONCLUSION

In its general conclusions, the committee says that all steps designed to minimise irradiation of human populations will act to the benefit of human health. Such steps include the avoidance of unnecessary exposure resulting from medical, industrial, and other procedures on the one hand and the cessation of contamination of the environment by explosions of nuclear weapons on the other. "The Committee is aware that considerations involving effective control of all these sources of radiation involve national and international decisions which lie outside the scope of its work." Here footnotes to the report give the text of alternative draft proposals put before the committee by the U.S.S.R. and India. The Russian view was that the data were sufficient to enable the committee to conclude that there should be an immediate cessation of test explosions. This proposal was rejected, Czechoslovakia, U.S.S.R., and the United Arab Republic voting for it and Belgium and India abstaining. The Indian wording was: "The physical and biological data contained in the report lead to the conclusion that it is undesirable to allow any general rise in the level of world-wide contamination because of its harmful effects and that any activity which produces such a rise should be avoided. Nuclear tests are the main source at present which produce such a rise." This proposal was also rejected: the voting was 5 for and 5 against, with 5 abstentions. At a press conference last week, Dr. Pochin said that the Russian draft implied that the committee had considered both the pros and cons of nuclear tests, whereas in fact only the cons had been within their terms of reference.

MANAGEMENT OF CHRONIC PSYCHONEUROSIS IN GENERAL PRACTICE *

C. A. H. WATTS
M.D. Durh., D.Obst.
GENERAL PRACTITIONER, IBSTOCK, LEICS

THE chronic diseases seen in this practice have been studied over the past fifteen months. All the permanent and the frequently recurring diseases are recorded. There are some 8000 patients at risk, and about a quarter of them have a chronic disease. Sometimes the disease is serious (e.g., cancer or tuberculosis); sometimes it is recurrent (e.g., asthma or peptic ulcer); and sometimes it is comparatively trivial (e.g., a lazy eye or psoriasis). Chronic mental disorders account for 14% of all the chronic patients (see table). This figure does not include the psychosomatic disorders, which account for another 30% of the chronic diseases recorded.

Far and away the largest chronic psychiatric problem in general practice are the psychoneurotics; they stem from three sources: chronic anxiety, inadequate personality, and unresolved depression. These types of case cannot be neatly pigeon-holed under clearcut diagnoses. The patients listed show, in many cases, a mixture of two or even all three sources. In other words, a patient with inadequate personality who cannot face the stress and strain of life may become anxious or depressed or both, and become permanently disabled. Unless the patient was known before he became ill, it is often impossible to pinpoint the cause of his illness.

These patients all have symptoms which worry them but have no adequate physical basis. Either their condition is permanent or they are so insecure that the least upset bowls them over, and, once ill, they take longer to recover than most people. They do not appear to respond to psychotherapy. If not constant attenders at the surgery, they are seen much more often than their more stable brethren. Some can work, and a few reach a high standard of proficiency in their work, especially the neurotic tidy obsessional housewives. Most are inferior workers, doing labouring jobs which they frequently change; absenteeism is rife, and many are permanently unemployed.

* From a lecture given to general practitioners at the Uffculme Clinic in Birmingham on March 19, 1958.

CHRONIC MENTAL DISORDERS IN A GENERAL PRACTICE

Illness	No. of males	No. of females	Total
Psychoneurosis	60	104	164 (56%)
Epilepsy	30	26	56 (19%)
Schizophrenia	12	10	22 (7%)
Amentia	12	5	17 (6%)
Alcoholic addiction	9	4	13 (4%)
Senile dementia	4	8	12 (4%)
Paraphrenia	1	3	4 (1%)
Psychopathic personality	4	..	4 (1%)
Compensation neurosis	3	..	3 (1%)
Total	135	160	295

When I first went to Ibstock fresh from a neuropsychiatric centre, I was full of enthusiasm and tried to help some of these patients by psychotherapy.

Case 1.—Mary was a single woman, aged 40. Her illness started at the age of 16, when spinal disease was diagnosed and she was put on her back for three months. Since then she has always had a "weak back", although no general practitioner or specialist has been able to explain the cause. From the psychological point of view she had enough to break anyone's back. She was an intelligent and very capable person, but at the age of 14 all hopes of advancement along her own lines went when she was drawn into the family business because of her mother's illness. The family were thrifty and hard-working to a degree of absurdity. Work and money-making were the only things that mattered. Social life was frowned on; smoking and alcohol were forbidden. At the age of 40 her mother still referred to her as a young girl and treated her as such.

After a few sessions there was a vast outpouring of hatred against her mother, with floods of tears. This psychocatharsis helped, but improvement was only temporary. For months I saw her periodically for a painful session of half an hour or more. She cannot improve, because she is in a hopeless trap until her parents die, and by then it may be too late. She has not the training, resources, or courage to go elsewhere. She cannot change either herself or her circumstances, and so she remains a chronic and troublesome neurotic.

Case 2.—Susan, aged about 42, was coaxed back to work after ten years on the club with a spurious label of thyrotoxicosis. She kept at work for a year or more and then relapsed, and I could not get her back to work a second time. She now has a certificate for nervous debility.

I tried my hand at several such problems, but with none did I achieve any lasting success. My senior partner is a first-class physician, but he claims to have no interest in psychiatry. Looking back over twelve years, I realise

that I have not cured a single chronic psychoneurotic whom he had failed to cure. I was able to help some for a limited time, but in the end I was defeated. I believe that, with more time, one might be able to help more of these patients; but the hours of work required are quite out of keeping with those available in general practice.

Some timid souls, however, are helped by repeated interviews and reassurance; they come to the surgery at short intervals for maintenance doses of the most simple psychotherapy.

Case 3.—Jill is an anxious woman who comes of a neurotic family. When her son contracted paralytic poliomyelitis, she developed a pathophobia for herself and her family. Any trivial complaint brings her to see me, and I encourage her to do this, because it is usually quite easy to listen to her story, to explain what is happening to her, and to reassure her. I do not think that she has the mental capacity for deep therapy, which might make her permanently more secure. She knows that I will always listen to her. She is better employed getting my opinion than that of the neighbours. I never deceive her; we understand each other.

Case 4.—Sybil is an attractive young woman, aged 27. She keeps her house like a new pin. She has been in trouble ever since I have known her. First she fell out with her parents and went to live with relations. Then she had trouble at work. Her next difficulty was with the landlord of her rooms after her marriage. After a year of misery she found a house, and then became depressed because no baby was coming along. She conceived soon afterwards, and her pregnancy was the best nine months I have known her to have. Indeed she has since admitted that it was the happiest time of her life. This island of contentment in a sea of anxiety and depression may be significant. She had an easy labour, and then troubles began with a vengeance. The baby would not conform, and both the health visitor and I were fearful at times for his life and hers. She saw a psychiatrist and electroconvulsion therapy was given, with only a doubtful response. She now felt that she was labelled and that the neighbours jeered at her because she had been to a mental hospital. "It doesn't matter where I go, I am in trouble. What is wrong with me?" she asks. I see a great deal of her, and although I seem to be unable to help her radically, she seems to be helped by maintenance doses of understanding, sympathy, and reassurance. I am the only person she can turn to in trouble. She knows I will always listen to her story, bear with her tears, and in general be a kind of safety-valve.

Ideally we like to feel that the psychoneurotic patient will respond to some talking type of treatment, improve, and cease to visit us. We aim at helping them over a crisis, so that they can stand unassisted on their own feet. This never happens with the chronic patient; talking may help a little but never cures. All the rules of formal psychotherapy are broken with this type of case. A placebo is often essential, sedation is sometimes useful, and repeated examinations are on occasions unavoidable.

One class of psychoneurotic looks to his bottle of medicine as an essential part of life; it is a kind of fetish. The colour, constitution, or taste does not matter, so long as it is the same each time. He has a kind of "apple a day" philosophy. "Three doses a day keeps the illness at bay."

Case 5.—Tom was a man, aged 60, when I first knew him twelve years ago. He was off work because of hypertension, but there never has been any evidence that it was really the source of his trouble. He has a bottle of the same mixture every two weeks. We always have a chat about gardening or grandchildren for five minutes, and then off he goes. This is a happy arrangement for both of us. I keep him well; he does not waste my time. We both enjoy the fleeting contact.

A rather more time-consuming patient is the one who likes to have a "check up" each time he calls to see the doctor. He has his coat off and his chest bare almost as soon as he comes into the surgery. He seems satisfied with the most cursory examination, but just feeling his pulse and looking at his tongue is not enough. He is really another version of the chap who must do his quota of press-ups and physical jerks each day to prove to himself that he is still fit. I think one must just accept it that the examination is just another form of placebo from which one can never wean the patient. A periodic examination of these people is desirable because it is rather upsetting to find that the old neurotic has developed an inoperable growth under one's very nose. They all have to die sometime, but it is as well to know when this is imminent.

Sometimes a drug helps the patient by easing nervous tension, and many of these patients cannot live comfortably without a sedative, a hypnotic, or one of the amphetamine preparations. This appears to do them little harm, and apart from an occasional drug rash I have seen no complications. We give phenobarbitone quite freely to epileptics year after year without a qualm of conscience, and they rarely come to any harm. True addicts are occasionally found. These people depend entirely on the drug, which they take in increasing doses, and withdrawal causes a violent reaction. This true addiction must be very rare. We in Ibstock have covered about sixty years of practice between us and have never had such an addict on our hands, although phenobarbitone and allied drugs are given frequently to the chronic psychoneurotics. Apart from the use of chlorpromazine in chronic or recurrent psychotics, I have found no use for modern tranquillisers. I certainly do not feel that anything more useful than amylobarbitone, amphetamine, and phenobarbitone has been produced so far.

There is little hope of changing the warped personalities of these people, but one can occasionally ease environmental stress. Sometimes a change of work is indicated. The hysterical man is often an ambitious fellow who, like many immature personalities, has an exaggerated idea of his own capability. He comes to grief trying to work beyond his capacity, and by persuading him to take a less exacting job one often helps him at least for a time. Occasionally a new house will make all the difference. It is well known how quickly slum dwellers can make a new council house into a pigsty; but this does not always happen, and I can think of families where the new house made a big difference. The help of social workers here can be most useful. Rotherham, in Yorkshire, was years ahead of most places when in the early 1930s it started and completed slum clearance. The rent collectors on the new estate were all social workers who had the skill and tact to advise the new occupants to keep the coal in the coalhouse and not in the bath, and so on, and the scheme worked, and very few slum dwellers did not improve in housecraft.

Patients with inadequate personalities respond well to suggestions, especially from a kindly parent figure. It is important to establish genuine good rapport and to become a good parent; then, even if they cannot be altered radically, the rates and taxes can be kept down by maintaining them at work as much as possible.

Case 6.—When old Dan comes along complaining of pains in his testicles, I know he will have at least a couple of weeks on the club. To begin with I bow to the storm, I listen sympathetically to his story, I sympathise, I establish myself in the position of the kindly parent. Once firmly in that position I begin to prepare him to go back to work; this awful news must be broken to him gently. It should never be "You must

start work tomorrow ", but rather " You will be all right by the weekend ". In this way Dan is levered back to work, and I suppose he does work for 10 months in 12, which is much better for the community than no work at all.

Advice on birth control may help the mother who is already overwhelmed by the size of her family. Unfortunately few of this type of patient have the wits or the self-control necessary to use it effectively. I tried to induce Sylvia to use a contraceptive sponge. I showed her how to use it, but she had a better method. She attached tapes to it and wore it like a sanitary towel and has had a further 5 children since I gave her that advice.

Depressives

Of all the patients we meet in general practice those who suffer from chronic depression are the most pitiful and, I think, the most trying. They have usually seen a long list of consultants whose advice has not helped to solve their problems. They may have seen a psychiatrist and had electroconvulsion therapy or refused to have it. They are usually not bad enough to be certified, but many have had months in mental hospital with repeated courses of electroconvulsions and even leucotomy; and none of this treatment has helped them. They are sick people, tearful, depressed, and depressing. They wreck all happiness in the home with their misery and self-pity. The general practitioner is left with a feeling " I have tried everything I know with this patient, and nothing helps, and I know of nothing I can do or anyone else can do to help ". The chronic anxiety and hysterical state can be jollied along with understanding sedative or placebo. Nothing appears to help the depressive, and there is always some risk, albeit small, of suicide. So far only one of my chronic depressions has successfully taken his own life. Some of these patients are reluctant to see a psychiatrist or to have electroconvulsion therapy. If such treatment has not been given it is well worth a trial in these cases, even after years of depression.

Case 7.—Martha was aged 36 when I first came across her. Her troubles had started at the age of 16, when a young man kissed her, and she was sure she would become pregnant. She came to me twenty years after this initial upset, depressed beyond words because she had missed a period. She was married and claimed to want children. She was not pregnant but she could not be convinced until nine months had elapsed. Thereafter, though she agreed that she was not pregnant, she remained a miserable and depressed hypochondriac. Talking did not help; and, although she saw a psychiatrist, she refused to have electroconvulsions. This went on for five long weary years until her sister-in-law developed a depression. The younger woman had electroconvulsion and improved so rapidly that my patient agreed at last to have them. Much to my surprise and relief she improved a great deal. She is not a robust normal person, but she is a pleasure to handle compared with what she used to be.

These patients seem to have no insight into their illness, and certainly no ability to help themselves.

Case 8.—Ruth was diagnosed as a depressive in 1948. She saw a psychiatrist, who suggested electroconvulsion therapy, but she refused to have it, and she was never certifiable. A year or two later signs of disseminated sclerosis emerged and she became even more depressed. Euphoria is supposed to be characteristic of disseminated sclerosis, but it was not in her case. Again a psychiatrist was consulted, but now it was decided that electroconvulsions were contraindicated by the organic lesion. She is seen once or twice every week. If a visit is missed, I am usually sent for. Never have I known a patient with so many symptoms. She is always tearful, wishes she was dead, wants to see yet another specialist, and says that surely there must be some cure for her troubles. One day I spent half an hour trying to explain the organic nature of her spasticity, and how sometimes one had to accept a disability. I explained how, if a man lost his eyesight through an accident, he could never grow new eyes, but he could adjust his life. I talked to her about Douglas Bader, and I felt most convinced by all my clever arguments. When I had at last finished she exclaimed, " Wouldn't it be nice if you could find a cure for me ? " and then she dissolved into tears.

Spouses should be allowed to unburden themselves and be encouraged by the knowledge that the doctor at least understands something of their troubles. In contradistinction to the patient the spouse often shows remarkable insight. This is well shown in the following case.

Case 9.—Elizabeth, aged 56, has been depressed ever since I went to Ibstock. She went to a mental hospital as a voluntary patient and stayed only five days. Her husband came to see me after Christmas last year to tell me how she had attempted suicide. He had gone to do some shopping and on his return found his wife in the rain-butt up to her neck in water. " If I had been going to do it I would have gone in head first," was his summing up. " I think she waited on the stool until she heard me coming up the passage and then she stepped into the butt just to try and hurt me, to create a scene." I think he was quite correct in his observation.

It is important to spot this depressed type of patient. They are very sick people in dire need of sympathy. They tend to get estranged from their families, and it is most important for the doctor to remain tolerant and understanding, even if he has little to offer by way of active treatment.

Conclusions

The general practitioner should not have to carry the burden of these chronic mental patients alone. He has useful allies in the district nurse, the health visitor, the duly authorised officer, and the clergy. He should make full use of their help. In our village the Townswomen's Guild have a rota of volunteers who befriend and visit all the chronic sick. This kind of activity on the part of the community should be encouraged and extended. Whether we like it or not, the psychoneurotic will remain on our hands until he dies or we die. If we can find ways and means of making our association more useful to the patient, we also make it more tolerable to ourselves. This section of the community is often a heavy burden on their doctors. Today the fate of the chronic mental-hospital patient is under serious review. The chronic mental patient in general practice is also a problem worth a good deal of attention and research.

". . . Another example of a new plague threatening us now in much the same way as cholera and typhoid used to in the past is injury and death from accidents . . . Accident death rates are not actually rising, except among the young men and the elderly; but they are not going down anything like quickly enough, and thus are becoming proportionately more and more important. Death and injury by motor vehicles particularly is now very nearly public health problem number one. The snag is that it does not lend itself easily to investigation. To begin with, the whole subject is fraught with emotion; people get terribly upset if you start asking them if they drive after having a drink or two (nearly as touchy as when you talk to them about smoking and lung cancer). That is half the trouble about the new plagues: in the old days the authorities could remove the pump handle and all would be well. In these days it is a matter for the individual: *I* have to change *my* habits of eating and drinking or driving or smoking, and that is much more difficult to do than to get someone else to lay on a clean water supply."—Prof. E. MAURICE BACKETT. *Listener*, May 22, 1958, p. 839.

Occasional Survey

THE FRONTAL LOBES AND HUMAN BEHAVIOUR *

HUGH JARVIE
M.D. Glasg., B.Sc. Oxon., D.P.M.
SENIOR LECTURER, DEPARTMENT OF STUDIES IN PSYCHOLOGICAL MEDICINE, UNIVERSITY OF LIVERPOOL

IT is but seventy years since the first observations were published relating changes of behaviour in man to lesions of the frontal lobes (Welt 1887–88). It is true that Harlow (1868) reported the case of a man called Phineas Gage who, after the passage of an iron bar through his head, showed a complete change of personality. Both frontal lobes were severely damaged in this man, but the association between the site of the wound and the appearance of the personality changes escaped Harlow; what interested him was the fact that the patient recovered from so grave an injury.

Welt's paper forms a definite point of departure; its title—" Concerning changes in character in man following lesions of the forebrain "—is clear and unequivocal. Three years later Oppenheim (1890) introduced the term *Witzelsucht*, which persists today as a kind of spurious hallmark of the frontal-lobe syndrome.

Many contributions have followed those early papers of Welt and Oppenheim. At first based upon the effects of frontal-lobe tumours, cortical degenerations, frontal-lobe injuries, and frontal lobectomies, they have in recent years largely been derived from the study of prefrontal leucotomy and its sequelæ. There is still, however, no generally accepted explanation why these frontal-lobe changes take place; and the changes themselves, and the conditions determining their appearance, remain ill defined. Moreover, changes in behaviour follow lesions of other areas of the brain, notably of the temporal lobes and the hypothalamus, and it is not yet known to what extent these changes are qualitatively similar to, or different from, those that follow injury to the frontal lobes. Bleuler (1951) said: " The so-called frontal syndrome is not characteristic of a frontal lesion but occurs also in most other brain lesions if they are localised."

It is certainly surprising to find that, when you have worked at a particular question for years, other observers consider that it does not even exist. I think that Bleuler's view is wrong; but the fact that it was possible for him to come to such a conclusion emphasises the present uncertainty.

Permanent Frontal-lobe Changes

What kinds of change in behaviour follow lesions of the human frontal lobes? To answer this question I will draw on the results of an investigation that I made into the intellectual and behavioural changes in 71 men with wounds of the brain (Jarvie 1954a, 1954b, 1956). In 46 of these men the frontal lobes were damaged.

The results showed clearly that certain permanent changes in behaviour took place only when the frontal lobes were injured. These changes did not take place in every case of frontal-lobe wound, but when they did they often had a particularly destructive effect on the personality. They did not appear at all in cases in which damage to a frontal lobe was only slight, and in only 9 of the 37 cases in which it was severe. The distribution of these changes among the 9 cases was as follows:

	Case no.	1	2	3	4	5	6	7	8	9
Restlessness		—	P	—	P	P	P	—	P	—
Increased drive		P	—	—	—	—	—	—	—	—
Stereotyped actions		—	P	—	—	—	—	—	—	—
Increased sexual activity		—	—	P	—	P	—	—	P	—
Talkativeness		P	P	P	P	P	P	P	P	—
Inappropriate talk		P	P	P	—	—	P	—	—	P
Impulsive actions		—	—	—	—	—	—	P	—	—
Emotional blunting		?	P	P	—	—	?	—	?	?
Loss of anger response		—	P	—	—	—	—	—	—	—

—, absent; P, present; ?, doubtful.

Restlessness

An increase in general activity as restlessness was noted in 5 cases and showed a remarkably consistent pattern: the man would move about, to and fro, perhaps following someone, in a way not dissimilar to the quadrupedal pacing after frontal-lobe ablations in the monkey. Alternating with the phases of restlessness were long quiescent periods when he stayed in bed.

Increased Drive

The restlessness usually made directed activity impossible or difficult; but in 1 case the change in the man's activity took the form of a well-coordinated increased drive, such as has previously been reported after frontal lobectomy (Ackerly 1935, Rylander 1939).

Stereotyped Actions

In the monkey stereotyped actions may be superimposed upon the basic pattern of quadrupedal pacing, the animal, for example, touching a feeding-box over and over again. Similar stereotyped actions are seen after wounds of the frontal lobes. One man, when given a pencil, began to scribble with aimless repetitive strokes, and it was not easy to stop him; another denuded an area of his skin with repeated scratching.

According to Denny-Brown (1952) these limited stereotyped actions seldom persist more than a month after the injury; yet similar actions were noted in 1 man in the present series seven years after he was wounded. When interviewed he had attacks of yawning; and he went on yawning as though he could not stop. He was also subject to " crazes ", when he would carry out certain actions repeatedly. Once it was cleaning shoes. " He keeps cleaning all the shoes in the house," said his father, " yet if he went to work in a shoe factory he would soon get tired of it."

Increased Sexual Activity

In 3 men there was an increased desire to carry out the sexual act; and they would solicit their wives persistently for this purpose, both by day and by night. With one exception these men made no sexual approach to women other than their wives. The exception was a man who had served several prison sentences for indecent exposure. This tendency to indecent exposure, like his generally increased sexual desire, only appeared in his personality after he was wounded.

Talkativeness

Increased talkativeness was a feature in 8 cases. In most of these it simply took the form of a loss of reticence rather than loquacity. These men would now butt into conversations, whereas before they were wounded they would have remained silent.

In other cases the talkativeness was more obvious, and the man would talk for long stretches at a time. There was no sense of pressure behind the talk, and these men could be interrupted, when they would listen quietly to what was being said without attempting to intervene.

Inappropriate Talk

In 4 of the men who showed increased talkativeness there was nothing offensive or inappropriate in the content of the talk. In the other 4, and 1 other in whom talkativeness could not be confirmed, the talk was continually, or frequently, inappropriate in one sense or another. This inappropriate talk showed many characteristics, being tactless, boastful, hurtful, crude, indiscreet, or sexual. Not all these characteristics appeared in each case; but in each man certain dominant themes were apparent.

Impulsive Actions

Foolhardy and impulsive behaviour was observed in 1 case.

* Paper read at a Symposium on the Frontal Lobes held in the University of Liverpool on March 22, 1958.

Emotional Blunting

Changes in the capacity of the man to react with normal emotion to ordinary human situations and events proved exceedingly difficult to assess in these cases. A few of the men whose behaviour was socially disturbing sometimes appeared to be emotionally unaware of the repercussions of that behaviour on others, but this was by no means invariable. This apparent lack of emotional depth was often difficult to reconcile with their emotional warmth in other directions—for example, in their relations with their wives and families. In the present series I was able to convince myself of the existence of a real degree of emotional blunting in only 2 cases.

Loss of Anger Response

There was complete loss of the normal response to anger-provoking situations in 1 man; it was impossible to make him angry, even by reviling him.

Other Changes

Not all the changes in behaviour that were noted after these frontal-lobe wounds persisted as permanent characteristics of the man's personality. In certain cases a decrease in spontaneously initiated activity was a striking feature in the weeks and months following the injury; but this might only be perceptible as a slight decrease in initiative years later. For example, one man, four weeks after he sustained a bilateral frontal-lobe wound, sat for over an hour with a thermometer in his mouth without raising any objection. Within a year he had returned to his former employment, and was so employed seven years later.

Emotional attacks, usually of laughter but sometimes of weeping, comparable to what Rylander has called " affective incontinence ", normally disappeared within a few months of the man's being wounded; this was also the case with the excessive appetite that was sometimes reported.

In none of the frontal-lobe cases was there convincing evidence of a striking, or sustained, elevation of mood, and certainly nothing similar to the spontaneous happiness and jocularity described as euphoria by Rylander (1939) in a high proportion of his cases of frontal lobectomy. A few of the men that I examined within a week or two of their being wounded looked euphoric because they had ruddy complexions, appeared exceptionally well, and smiled rather freely. In these cases, however, there was no subjective change of mood in the direction of elation, or such change was slight. This appearance of well-being was regarded as being due to a temporary stimulation of those autonomic mechanisms that are known to be located in the basal parts of the frontal lobes and the anterior temporal region.

Incontinence of urine was not confined to the men with frontal-lobe wounds; but in such cases its incidence was higher, and it was usually present for a longer time than when the wound was restricted to other areas of the brain.

Explosive outbursts of bad temper were equally common in cases in which the frontal lobes were injured and in those in which they were not. In many instances this explosiveness tended to persist, but it often became less prominent as time went on.

Some Explanations

It is difficult to imagine that so diverse a series of changes could ever have been regarded as due to a single cause; yet two explanations of this kind have been put forward to explain the frontal-lobe changes.

Scarring

One of the explanations is that the changes are due to epilepsy resulting from the scar that forms after the wound. This view was favoured by Hebb (1945, 1949). Hebb and Penfield (1940) described the case of a man with an epileptic behaviour disturbance due to a scar on the frontal lobe whose behaviour was greatly improved after frontal lobectomy.

In the present series at least 1 of the 9 men who showed permanent changes of character began to show changes of this type almost as soon as he recovered consciousness, and before any scar could have been formed, and epileptic attacks have not been recorded at any time in 4 of these men since they were wounded. In view of this it is difficult to see how these personality changes could be due to epilepsy unless the term is extended far beyond its legitimate usage.

Intellectual Deficit

Goldstein (1923, 1936, 1942) considers that damage to the frontal lobes causes a single basic intellectual deficit on which all the subsequent deviations in behaviour depend; the essential nature of this deficit is the loss in the capacity to abstract; in the intellectual sphere this is shown by the inability of the patient to grasp the essentials of a situation, either in a practical everyday setting or in certain special tests—the Goldstein-Scheerer sorting tests (Goldstein and Scheerer 1941). This deficit is not limited to conceptual tasks but affects general behaviour also. The patient is able to grasp only part of a behavioural situation; hence his approach to it is faulty, and in consequence he acts inappropriately.

It is not difficult to discover from whom Goldstein's views are derived. It was Hitzig (1884) who, having confirmed the " silent " nature of the prefrontal areas by their lack of response to electrical stimulation, suggested that they were concerned with " abstract thinking ".

The view that frontal-lobe damage causes loss of the capacity to abstract could not be confirmed in the present study. All the men were examined with standard intelligence tests; tests that test processes of abstraction to a high degree. Of the 9 cases with permanent changes of character intellectual deficits could be demonstrated in only 3, and in 2 of these the intellectual impairment was doubtful.

I did not use the Goldstein-Scheerer tests in this investigation; but recent experience of these tests in examining brain-injured people has convinced me that deficits would be demonstrated on them only in cases in which they could also be demonstrated by more conventional tests.

It is still widely held that the frontal lobes are intimately concerned with intellectual function. Knight and Tredgold (1955) speak of avoiding damage to the " intellectual pathways " in the operation of orbital leucotomy to minimise personality changes. Even Rylander (1939) believed, at least in part, that the personality changes were due to some kind of intellectual change. He considered that changes such as tactlessness were partly due to euphoria (not a prominent feature in the cases that I have described) and partly due to a " slight blunting in the higher and more differentiated feelings upon whch the social and ethical deportment is founded ", but he also thought (paraphrasing Goldstein) that they depended " upon a certain intellectual incapacity to adapt oneself to the situation and to correctly appraise how one's remarks are received ".

In the cases that I have described many of the men were fully aware of the change in their behaviour; they could give an account of it and were often emotionally disturbed by it. It was therefore impossible in these cases to show that the personality changes depended either on emotional blunting or on a lack of intellectual awareness of the changes that had taken place.

I know that mental tests are imperfect instruments, and there are aspects of human intelligence that are far beyond their capacity to assess. Mental tests are, however, the best means available for measuring objectively human intellectual function. If we are going to continue in the

belief that the frontal lobes are some kind of special intellectual organ, we must be prepared to find a valid test that will demonstrate these presumed intellectual changes. I think that the word " intellectual " is a bad one to apply to these personality changes, and there are more accurate ways to describe them.

It is clear that there must be some anatomical basis for these changes—some essential anatomical conditions to be fulfilled before the changes appear. Some of the changes, such as the diminished spontaneity and increased appetite, might well be consistent with a general disturbance of frontohypothalamic coordination; and it has been suggested that the restlessness, which is so striking in man and the monkey, is due to damage to the caudate nucleus rather than to the frontal lobe (Davis 1951, Turner 1957).

I do not think, however, that these changes can depend to any great extent on the amount of frontal-lobe tissue destroyed, as suggested by some workers (Frankl and Mayer-Gross 1947, Meyer 1950). In the first place they may not be very obvious even after bilateral frontal lobectomy, and it is clear from recent reports that they are appearing after limited frontal-lobe operations such as cingulectomy and orbital leucotomy (Tow and Whitty 1953, Tow and Lewin 1953).

So far as I am aware, the men that I examined in the present series are still alive, and, in the absence of pathological studies, it is clearly impossible to draw any accurate anatomical conclusions from this material in spite of the excellent radiological and surgical evidence available. The only conclusion that I would draw is that these changes took place, so far as I could tell, in cases in which only one frontal lobe appeared to be damaged; and this observation is consistent with the appearance of similar changes in the few reports of unilateral leucotomy that have been published (Margolis et al. 1952).

Previous Personality

It has long been known that distinctive personality changes follow in only a small proportion of cases with frontal-lobe damage. Feuchtwanger (1923) recognised this when he studied brain-wounded men from the 1914–18 war, and in the cases that I have described personality changes of a distinctive type appeared in only 25% of the men with severely damaged frontal lobes.

Now this is a most significant fact, and I do not think that the explanation of it can be wholly anatomical. It seemed to indicate that the men who developed behaviour changes were in some way different from those who did not, and that the difference might lie in the personalities of the men before they were wounded. Part of my investigation was therefore directed to a study of the normal personalities of the men who showed significant personality changes.

The men had all been brought up in family situations that could well have affected the way in which their personalities developed. Often one parent was dominant, while the other was a cipher. In childhood they were seldom allowed to express opinions of their own; so, when they grew up, they would rarely enter into conversations or assert themselves. " I would walk away rather than get into an argument with anyone," one of them said, " I wouldn't say boo to a goose." They appeared, at least superficially, to be quiet and inhibited in temperament; hence it was not surprising that their parents looked back on them as model children.

It cannot be doubted, however, that conflicts existed beneath the quiet exteriors. These men must often have wanted to rebel against the prohibitions of their environment by making cutting remarks or to overcome a sense of inferiority by boasting—elements that now appear all too obviously in their present behaviour. The man whose talk was almost entirely sexual was preoccupied with sexual matters before he was wounded, although he was regarded by his father as " rather prudish and not interested in sex ". The sexual talk was not just talk that happened, not just obscenity; it represented the now open expression of a conflict that was previously concealed.

In these men with damaged frontal lobes certain features in their personalities that were formerly kept under control come to the surface, as though the braking power in respect of these features had become less effective. This was well understood by most of them. " It's out before I can stop it," said one man referring to his tactlessness.

We are all aware of this braking power in relation to our own behaviour. Many of our behaviour patterns are formulated at a subconscious level before they are allowed active expression as speech or other motor acts. These patterns, however, are subject to a process of judgment when their appropriateness or otherwise is assessed before they are translated into action, either completely, or in a modified form. Often it is only after a pattern of behaviour has been executed that we know that it is in some way different from that originally formulated. We are aware, for example, of something that we were about to say but only realise, when we have not said it, that it would not have been appropriate. After frontal-lobe damage certain inappropriate features may be facilitated and gain motor expression before they can be modified.

Now this loss of inhibition is a very characteristic thing and probably depends exclusively on interference with the normal functioning of the prefrontal cortex. It does not extend to every part of the man's behaviour but only seems to occur in relation to those aspects over which the man had to exert a special vigilance before he was wounded, these aspects in turn depending on his personality.

Frontal-lobe Behaviour

I have tried to show that, after lesions of the human frontal lobes, certain striking changes in behaviour take place which are susceptible of explanation.

When I look at this case material again I wonder what I have missed; there remain many facets of frontal-lobe behaviour that puzzle and intrigue me. Why should disinhibition affect only certain aspects of the man's behaviour? Does this mean that we have now to consider different types of frontal-lobe organisation in different people depending on their environmental experiences? Why is so much frontal-lobe behaviour stereotyped and repetitive—not only the isolated stereotyped acts, but also the talk, the sexual behaviour, and the restlessness? Why did the man who had lost much of his capacity for emotional response look so youthful? A youthful appearance was noted by Rylander (1939) in some of his cases of frontal lobectomy. Was it that, being deprived of the emotional repercussions of living, he aged more slowly than we who are continually subject to them?

Today we seek our understanding of brain function among strange arts. We think of it in terms of the mathematical arrangements of nerve-cells (Sholl 1956), or we look for explanations in the working of calculating machines, or in the gyrations of mechanical animals. No doubt the originators of such theories have an ingenuity of mind that few of us possess; but I cannot help feeling that the answers to our questions about the functions of

the human brain will not be found in that way but as they have always been found—in the careful collection of clinical facts and their pathological correlations.

The investigation upon which this paper is based was carried out during the tenure of a Beit Memorial Research Fellowship, in the department of neurology, The Radcliffe Infirmary, Oxford, and I am indebted to the head of that department, Dr. W. R. Russell, for the facilities received.

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Public Health

Chemical Preservatives in Food

THE nutrition panel of the food group of the Society of Chemical Industry met on April 9 to discuss chemical preservatives.

Dr. M. INGRAM said that the most commonly used, and at present the most important, chemical preservatives are benzoate, sulphur dioxide, and nitrite. All are weak acids, and in each case the undissociated acid is the active preservative; hence, as the pH rises, so does the amount of preservative needed to give an active level in the product. All are therefore more active in acid than in neutral substances.

Benzoic acid has no odour and no taste and is not volatile, but a fair amount is needed in non-acid materials. It is antimicrobial and has no other known effect.

The situation is rather more complex in the case of sulphur dioxide. The active agent is undissociated sulphurous acid; but, besides dissociation, a series of reversible compounds is formed with sugars such as glucose and other aldehydes (but not with the dissacharide sucrose), greatly reducing the concentration of the active fraction. A high limit of 2000 parts per million of sulphur dioxide is set for cordials that are to be diluted. A limit of 1500–3000 p.p.m. is set for pulps for jam making, where sulphur dioxide is lost by volatilisation in boiling; the several equilibria in such systems containing sulphur dioxide require time for their adjustment. Unlike benzoic acid, sulphur dioxide has other properties—it is a bleaching agent, and inhibits the formation of brown products in food.

Nitrite, usually as sodium nitrite, is widely used to cure meat; 200 p.p.m. is the maximum but more may develop naturally from the reduction of nitrate. Primarily, nitrite is used to give a good colour but it may have some preservative effect.

Sodium diacetate, propionic acid, and sorbic acid have all been proposed for various purposes, but their use is not yet allowed in this country. The use of esters has been suggested, but, although many are potent preservatives, they often have pungent odours and are of low solubility.

About £10 million pounds' worth of fruit pulp and juice is used in this country in the food industry each year, and storage and transport and handling of this amount of material is rendered possible only by the use of preservatives. The attraction of the antibiotics and of atomic radiation is that they may be able to do for the neutral foods what the chemical preservatives have done for the acid ones.

Dr. J. M. BARNES said that preservatives must by definition be toxic to some forms of life. The degree to which they are exposed and qualitative differences in susceptibility account for the death of offending microorganisms while the consumers' tissues escape injury. Toxicity tests to evaluate the safety of preservatives must include those assessing the effect of any reaction products formed between the food and the preservative.

Benzoic acid has been extensively studied. It is quantitatively excreted mostly after conjugation with glycine. Up to 4 g. has been taken daily by men without ill effect; the margin of safety is therefore very great. Sulphur dioxide (or sulphite) has been studied in rats, rabbits, dogs, and man. Large doses cause vomiting and abdominal discomfort. There is no evidence of any specific reaction to smaller doses.

Nitrites, if absorbed, can convert hæmoglobin to methæmoglobin. Of the less well-known preservatives, propionates and sorbic acid are metabolised through normal pathways and are probably harmless. Borates are undoubtedly toxic and probably cumulative; but the toxicity of formates or formic acid, and of formaldehyde in dilute solutions, is probably much less than has sometimes been assumed.

Mr. H. AMPHLETT WILLIAMS cited work by E. C. Wood which suggests that until a baby is about 6 weeks old it does not produce sufficient gastric hydrochloric acid to inhibit the growth of nitrate-reducing bacteria in the stomach. Nitrate can thus be reduced to nitrite, which can be absorbed with the formation of methæmoglobin. Much water is taken in reconstituted milk, and as little as 30 p.p.m. of nitric nitrogen in the water-supply is now regarded as potentially harmful for infants.

Medicine and the Law

Death after Poliomyelitis Inoculation

ON Aug. 9 a verdict of death by misadventure was returned by the Manchester City Coroner, Mr. G. J. Pycroft, on a girl aged 2, who had been given an injection of American Salk poliomyelitis vaccine on May 27 and a second dose on July 5.[1] The mother noticed no ill effects, but on July 9 the child bumped her head and three days later she died in hospital.

Dr. Leslie White, the pathologist, said there was no sign of injury but the brain and spinal cord showed acute signs of poliomyelitis infection. He did not connect the injections of vaccine with the child's death, because of the time relationship to the fatal illness (the incubation period for poliomyelitis normally being one to two weeks) and because of the absence of any similar incident in other children injected with the same batch of vaccine. It was not possible for one dose to be infected and the remainder to be free from infection.

The coroner said he must accept the medical evidence, but personally he would have thought there was a strong possibility that the child's death was connected with the second injection of vaccine.

Commenting on the inquest,[2] a Ministry of Health spokesman said that the Ministry was not aware that any batch of vaccine issued in this country had proved unsafe. Emphasis had always been laid on the fact that vaccination did not guarantee complete protection against the disease. Between the start of the vaccination programme in 1956 and the end of July, there had been 35 cases in which poliomyelitis developed within thirty days of inoculation, and with 2 exceptions these were all children. During the same period over 6 million children had received two injections of poliomyelitis vaccine.

1. *Manchester Guardian*, Aug. 8, 1958; *Birmingham Post*, Aug. 8.
2. *Manchester Guardian*, Aug. 9.

In England Now

A Running Commentary by Peripatetic Correspondents

" No, George," I said firmly into the telephone. " I admit that I often don't know what files are in my In-tray, still less in my Pending; but I've just been down to the Eocene layer—there was a faint outline of an ichthyosaurus between the two bottom files—and I can say with confidence that I have not got your file ' Senior Registrars, beards, long, white, as a distinctive mark of '."

When we met at lunch, George asked if I remembered old MacPrendergast. " When he retired he decided to go through all the files in his trays. The bottom one, to his surprise, seemed faintly familiar, and he remembered that when he first joined us he had seen a letter dealing with St. Botolph's Hospital for the Rising of the Lights, and had called for the papers. The last patient, he found, had been admitted in 1820 following George IV's coronation, and the Turnover Interval before that had been 17 years. Being young and enthusiastic he had decided that, even if no other achievement could be set to his credit during his career in the Department, he would at least close this useless and redundant lazar-house. After a bit, of course, he lost interest and anyway was transferred to Establishment, but now it all came back. Digging down through the file, he soon passed into the longhand era and farther back to the long *f* for s. (' Pa*ff*ed to you plea*f*e ').

" The black letter stumped him a bit but he managed to decipher that Thos. Cromwell made it a condition of not being nationalised at the Dissolution that St. Botolph's should also admit cases of the Mother and the Wolf, Tissicks, Purples, and Livergrown, as well of course as Rising of the Lights.

" He got quite excited over a 14th-century minute with a date-line ' Januarie 1390 ': ' Pleynte is made and y-written y-wis that in this maysondewe highte sëynte Botolphe ther be scantness of mete save onlie for the Boarde of Governaunce.' Chaucer was a Civil Servant; could he have written this himself? But soon he was back to a document on vellum with cheerful little illuminations of Lords of the Treasury and other queer creatures which was a draft reply for the Abbot to put up to the Archbishop suggesting that since Botolph had been a local boy who made good, and since, moreover, a Pædiatric Department had been added as a war memorial after the Senlac ' incident ' —it was politically tactless to talk about the Norman Conquest —the local outcry (*clamitatio vicinorum*) at closure would be so great that the Archbishop might wish to say that the matter was still under consideration. My Lord Abbot inserted the word ' active ' (*vivida*) before ' consideration ' in the draft but otherwise nothing seemed to have happened. But MacPrendergast wasn't satisfied. He had at the back of his mind that there had been earlier letters—much earlier—and that in a moment of depression he had slipped them behind his bookcase. There were earlier letters: but unfortunately he had put them on top, not behind his bookcase; and, as they were stone tablets cut in runic characters, when he moved the bookcase. . . . . Well, poor old MacP. never lived to draw his pension.

" St. Botolph's? Oh, still going strong. Of course he never had a hope of closing it. Children, and all that. And yet they used to say the National Health Service would destroy local interest and patriotism about hospitals!"

* * *

Beyond a vague belief that doctors could not be the only people excused from jury service, I have never known who else shared this privilege or disability with our profession. A wrong address has just brought into my hands a summons to jury duty which includes a " List of Persons entitled to Exemption ". It begins grandly enough with " Peers—Judges—Sheriffs—Provosts " (this is a Scottish list). We come near the middle, between " Keepers of Prisons—Professors in Universities " and " Certified Midwives—Officers and men . . . *on full pay*." (Physicians and surgeons, like advocates near the top of the list, must be *practising*, though oddly enough this does not apply to dentists.) The list ends with " Income Tax Commissioners—and Lighthouse Keepers ". Truly we are in distinguished company.

* * *

I fear that my peripatetic colleague (Aug. 2) is overhasty in his condemnation of plastic, for sessional crises were not unknown even before its use.

Some twenty years ago, when seats were still substantially constructed in wood, a doctor and his wife went to a dance leaving their small child with a student as a sitter-in. On their return they could not find the young woman in any of the ground-floor rooms. Rushing upstairs they saw to their immense relief that the baby was sleeping peacefully; but strange noises were coming from the bathroom. The horrified doctor immediately remembered that he had varnished the seat that afternoon and had forgotten to mention it to their visitor.

When the door was burst open, it was at once clear that his fears had considerable substance. In his best professional manner, he reassured the sobbing and slightly hysterical girl and told her that her freedom was only a matter of moments. After two unsuccessful tugs he made a third very powerful heave, lost his footing, fell heavily to the floor, and broke his leg.

The situation was now serious; further professional aid was sought in the form of a plumber, who in his wisdom attempted nothing heroic but quietly unscrewed the seat. An ambulance was summoned and conveyed the doctor, the girl, and the seat to the local infirmary where they were admitted to the appropriate surgical wards.

According to an apocryphal postscript, the house-surgeon felt that he was too inexperienced to deal with such a complicated female case and left her for his chief's operating list in the morning. Eventually the anæsthetised patient (seat still in situ) was wheeled into the theatre, and the surgeon, turning to a postgraduate student notorious for his omniscience, said " Have you ever seen anything like this? " " Yes, Sir," was the reply, " Many times, but I have never seen it framed."

* * *

I remember reading about the use of body marks (congenital and acquired) for purposes of identification after some disaster; and I seem to remember, too, that textbooks of forensic medicine dilate upon the subject. But the Police had no trouble at all in identifying a nonagenarian who dropped dead on our Transport Department steps. In his pocket was a medical certificate given by me half an hour earlier, testifying that he was fit to drive a car.

* * *

As headlines screamed " Paratroops fly into Amman " and " G.I.s land in Lebanon ", I settled down to twenty-one days' terminal leave, probably the most recent " demobee " from the R.A.F. In fact, the ink was still wet on my signature agreeing to serve for the specified time on the Reserve of Officers—rather a formality, as I was automatically transferred. Still, I appreciated the polite gesture.

Cabinet Ministers drove into Downing Street, through a litter of photographer's flash bulbs, engines warmed up on airfields all over the world, the Navy put to sea, soldiers staggered from Q.M. stores under mounds of tropical kit, and I arrived home to find an ominous, official, O.H.M.S. letter waiting for me. This was it! No sooner had I managed to get out than they wanted me back. By tomorrow I would be swinging on a parachute, dodging noisy bangs from bad-tempered Arabs. I squared my shoulders and firmly opened the envelope. If my country needed me to defend the Commonwealth, NATO, the Baghdad Pact, UNESCO, and the Sack Line, who was I to hesitate to answer the call. After all, my best blue was still almost new.

" Dear F/Lt.," I read, " Your Personal Clothing Card Form 667B shows that you were issued with two coats (Coats, White, Medical Officer) on Jan. 23, 1957. Please return same as soon as possible or a cheque for thirty shillings to cover Form 664B action."

Letters to the Editor

CHILDREN IN HOSPITAL

SIR,—Your editorial of July 26, What Hospitals for Children? contains such a burden of special pleading and so many mis-statements in regard to infectious hospitals that it cannot be allowed to pass without challenge. First you state that these hospitals are full of children suffering from non-infectious diseases. Quite shortly and simply, this is not true. Then you complain that they take cases of, "pneumonia, meningitis . . . and gastroenteritis." Why not? Must I remind you that pneumonia and meningococcal infections are notifiable diseases for the reception and treatment of which infectious hospitals were expressly set up and which they are obliged to admit if requested. Gastroenteritis too is notifiable in many areas and, in my experience, is sometimes almost as infectious as measles. Where else should it go?

Your proposals are certainly drastic and simple. You would prohibit the admission of children to adult wards, close childrens' wards in general hospitals, small pædiatric units, and fever hospitals, and decant their contents into a small number of big pædiatric units duly equipped with cubicles which are to be set up at some unspecified date. I will not dwell on the arrogant and naïve assumption that pædiatricians could take infectious diseases in their stride, but even if they could there are a few practical considerations to be taken into account. Normally in my unit, and those I visit, at least half the patients are adults, and if the dividing line be placed at 10 years, the proportion would be considerably higher. What is to happen to these patients when the fever hospitals are closed? No doubt the pædiatricians of their charity would be prepared to treat them, but that one feels would be to subject their principles to an unbearable strain.

This gibe may sound trivial or unworthy but it serves to underline why so many of us regard pædiatrics as the most artificial of the specialties. A small nucleus of genuine *expertise* in the management of the first years of life has been inflated beyond all reason or recognition. Thus Dr. Lawson (Aug. 2) tells us he has 550 beds "fully staffed and equipped to deal with *all* types of cases at all ages from 0 to 16" (my italics), and makes no bones of his conviction that no other hospital should be allowed to admit cases in that age-group while he has an empty bed. Could prerogative go further?

But in any case your proposals represent a retrograde step. One of the least disputable advantages of the National Health Service is that it has brought the consultant to the patient even in the remotest village. No matter how small the hospital, there is now no difficulty in obtaining the opinion of a neurologist, a dermatologist, a surgeon—or a pædiatrician—as required, and there can be no doubt that this has resulted in vastly improved standards of care. Your "small number of big pædiatric units" must be not only few but far between. Do you seriously suggest that the parents of a child with whooping-cough or dysentery should have to make a journey of 10 or 20 miles to see him—daily of course? If so, then I am constrained to ask, for whom do you think the hospitals exist—for the public or for the doctors who staff them?

By all means let us have big units for special treatment and facilities for X-ray, better bacteriology and virology with an ever closer liaison between all hospitals, general and special The historical separation of the general from the fever hospital has not been a good thing for either, but there was one particularly cogent reason why the fever hospital was relegated to the nearest mountain top surrounded with a stout high wall —to wit, smallpox. And unfortunately that threat still exists; indeed, if air travel continues to become cheaper and speedier so that tours to the smallpox areas become commonplace, importations of smallpox are bound to increase. Then we may have repetitions of what happened in a large London general-cum-fever hospital some time ago. There, some 700 beds were put out of action and more than 1000 persons set at risk by a case of smallpox disguised as chickenpox and, had not the disguise been penetrated so promptly and the situation handled so competently, grim consequences might have followed as they did at Brighton in 1951. The question is not so simple as it might appear.

The truth is, Sir, that, thanks to convergence of scientific and social factors, the centres of gravity in medicine are changing rapidly as we in fevers know to our cost, our beds in the London area having been cut by 90% since 1939. Pædiatrics, it seems to me, must also cut its coat according to its cloth and grin and bear its cross as best it may. Like us in the infectious world, pædiatricians have wrought so well as to imperil their own survival and though this may represent a personal tragedy to many of us, we can scarcely deplore it since undoubtedly from the national point of view it is a matter for rejoicing.

South Middlesex Hospital, Isleworth, Middlesex. G. E. BREEN.

SIR,—I should like to record my admiration of Professor Illingworth's many years of work on the problems and needs of children of all ages under hospital conditions; problems which he has felt profoundly and now sums up in his lecture to the Central Council for Health Education published in your issue of July 26. His level-headedness in this subject, which has so many emotional undercurrents, is a great asset, as the reforms which his criticisms indicate are the more acceptable, particularly to those with power of administration. But I would like to go on to support the plea made by Dr. Jacoby (Aug. 2) that "daily visiting is not a target to be aimed at but something to be discarded as insufficient for this purpose" particularly, I would add, for the under-fives. Sir James Spence told the pædiatric world for many years that mothers were good nurses (not only for babies). The Pickerills at Auckland showed that nursing by the mother reduced cross-infection. But although there is widespread acceptance of the truth of these ideas, a general disbelief in their practicability prevails. In the pædiatric units of the hospitals of North Bucks (which include an isolation unit) we have nevertheless in the last few years admitted mothers with rather more than half of the children under five. Visiting has in the same period gradually become completely unrestricted. Professor Illingworth is right to emphasise that we should be cautious about taking a mother away from other children at home, but from the evidence our mothers have supplied and that of other non-psychiatric outside observers, we feel satisfied that the mental health of children left at home has not been jeopardised.

When we admit the mother with the child we are in a sense taking on two patients instead of one. She also has her needs, as has anyone in strange surroundings and with a worry on their mind. These needs must be met by the pædiatric staff who (to borrow a word quoted in your leader from the Royal College of Physicians report) are "attuned" to the special needs of the *mothers* of sick children. This state of attunement of the staff at all levels, above all of the ward sister, comes only by experience built on an initial attitude of accepting the necessity for the mother to be there. The magnitude of this need,

or, as some think, its relative unimportance, is one of the main points of controversy at present. The need is seen by many to be fundamental for the under-fives, certain over-fives, and any child with cerebral palsy or mental defect who may have to be admitted to hospital. Keeping the mother with the child, when properly managed, certainly provides the best solution for the small child's special difficulties and stresses.

This is something that can make a big contribution to the welfare of small children in hospital, but Professor Illingworth mentions the subject extremely briefly (about 1/36th of the whole article), and avoids embarking on the controversy. That perhaps was wise, in that his paper as it stands is an authoritative contribution on the total welfare of the unaccompanied child in hospital. He does, however, state that "the arrangement presents great psychological advantages to mother and child". Endless examples might follow this statement. There is one I should like to give as it concerns attitudes and prejudices. It is that when the operation or treatment is over and the time comes for the child and mother to leave the ward, we feel we know them both better as people, better than we know an unaccompanied child and visiting parent. They also understand us and our purpose better. A psychological advantage has certainly been gained.

Stoke Mandeville Hospital, Aylesbury. DERMOD MACCARTHY.

SIR,—Certain of the statements made in Dr. Lawson's letter of Aug. 2 cannot be allowed to go uncorrected. It is quite wrong to say that the South West Metropolitan Regional Hospital Board proposes to close Queen Mary's Hospital within the next few months; the position is that the Ministry has requested the board to examine the practicability of transferring the Fountain Hospital to Queen Mary's.

It is true that the Board has no formally appointed pædiatric adviser or committee; but in this, as in other specialties, the practice is to invoke ad-hoc advice when necessary, as was done in March, 1957, when Prof. Alan Moncrieff was asked to take part in discussions which then resulted in the decision to continue Queen Mary's as a 550-bedded children's hospital. This manifests the inaccuracy of Dr. Lawson's statement that the Chairman of the Board refused to consider the use of expert advice, and also that the Board has never shown any serious interest in the provision of beds for pædiatrics.

The Board must now proceed to examine the proposal as requested by the Ministry, but the situation will not be helped by the publication of inaccurate and intemperate statements.

South West Metropolitan Regional Hospital Board, 11A, Portland Place, London, W.1. E. G. BRAITHWAITE.

ORAL TREATMENT OF PERNICIOUS ANÆMIA

SIR,—We were interested to read Professor Castle's comments (Aug. 2) on our article.[1] His main criticism appears to be that similar results might have been obtained had crystalline vitamin B_{12} been given orally in the same dosage, instead of the vitamin-B_{12}-peptide complex. If this criticism were really valid, then surely the problem of treating pernicious anæmia by oral therapy would have disappeared ten years ago with the discovery of the crystalline vitamin in 1948, for our *average* daily dose over the first eighteen months' treatment has never exceeded 14 μg. It has, we think, been clearly established both that absorption of the crystalline vitamin when given by mouth is only about 1% in the pernicious-anæmia patient,[2] and also that the daily body requirement of vitamin B_{12} is between 1 and 2 μg. This being so it seems to be an inescapable conclusion that a daily oral dose of the order we have given would have been completely inadequate to maintain a patient in health, unless the absorption of the vitamin-B_{12}-peptide complex had been considerably greater than 1%.

In passing, it is perhaps of interest to mention that in an American drug magazine where our findings are criticised on one page in terms similar to those used by Professor Castle,[3] on a different page in the same issue it was stated by another author[4] that although "small doses (1–2 μg.) of vitamin B_{12} are effective in causing remission" (when given parenterally) "500–1000 times as much vitamin is required when given orally". Professor Castle wishes both to retain his belief in the intrinsic factor, and also to claim—by inference—that an average daily dose of 14 μg. might in any case be sufficient to maintain remission, even if intrinsic factor were absent. If this is true, then intrinsic factor—assuming it exists—must be rather an inert substance. We cannot help feeling that Professor Castle, by making these two claims, is wanting both the half-penny and the gingerbread.

Furthermore, we cannot share his complete confidence in short-term responses as judged by serial reticulocyte counts, no matter how carefully these are carried out. In our view, there are so many variable factors influencing a reticulocyte response that it should not, in itself, be regarded as the ultimate index of the efficacy of any preparation. The only completely reliable test of any new product for the treatment of pernicious anæmia is that of time.

We humbly recognise the great debt which all hæmatologists owe to Professor Castle for his work on pernicious anæmia. We are, in fact, largely restating his original view[5]—which he now appears to discard himself—that pernicious anæmia is due to a failure of proteolysis. However, our reason compels us increasingly to reject the belief in intrinsic factor, as currently understood. New cases of pernicious anæmia are not common, and the work we have already published[1] was based merely on the first 6 cases investigated. We have now accumulated considerably more evidence which we shall publish in due course, and which, up to the present, in no way conflicts either with our published results, or our interpretation of them.

St. Helens Hospital, Lancashire. F. S. MOONEY
J. G. HEATHCOTE.

ATHEROSCLEROSIS AND ITS CEREBRAL COMPLICATIONS IN THE SOUTH AFRICAN BANTU

SIR,—We should like to refer to the letters from Professor Becker[6] and Mr. Walker and Dr. Simson.[7]

Talking of apoplexy, Boyd[8] says "two factors are always associated, namely, high blood pressure and arterial degeneration . . . the arterial lesion is nearly always an atheromatous patch. It is doubtful if hæmorrhage can occur from a healthy vessel no matter how high the blood pressure." Russell Brain[9] and Fishberg[10] hold substantially the same views. For this reason we were content to quote only one case of apoplexy listed by Becker[11] under "atherosclerosis". At that time we

1. Heathcote, J. G., Mooney, F. S. *Lancet*, 1958, *i*, 982.
2. Ungley, C. C. *Nutr. Abst., Rev.* 1952, **21**, 11.
3. *Drug Trade News*, 1958, **33**, 75.
4. Miller, O. N. *ibid.* p. 46.
5. Castle, W. B., Townsend, W. E., Heath, C. W. *Amer. J. med. Sci.* 1930, **180**, 305.
6. *Lancet*, 1958, *i*, 1019.
7. *ibid.* p. 1126.
8. Boyd, W. Pathology of Internal Diseases. London, 1944.
9. Brain, W. R. Diseases of the Nervous System. London, 1955.
10. Fishberg, A. M. Hypertension and Nephritis. Philadelphia, 1954.
11. Becker, B. J. P. *S. Afr. J. med. Sci.* 1946, **11**, 1.97.

did not realise that Becker had listed another 33 cases under a different heading in an earlier article. We regret having failed to quote all Becker's cases, but we consider the important point to be that Becker agrees that " on occasion the Bantu can and does develop just as much atherosclerosis as the European in South Africa ". We consider his estimate of the incidence of apoplexy to be too low and would agree with Walker and Simson's figure [7] of 3–4% for the Bantu in Johannesburg. We cannot agree with Walker's statement [12] that only 19% of Bantu show aortic atherosclerosis at necropsy.

In regard to the points raised by Mr. Walker and Dr. Simson we omitted to mention coronary disease in our article [13] because we intend to devote two further articles to this problem. An early note on our views appeared in your columns last year.[14]

Much of the misunderstanding which has arisen regarding the Bantu is due to the fact that his relative freedom from myocardial infarction has been attributed to a freedom from coronary atherosclerosis. It must be remembered that coronary thrombosis is only one of several manifestations of coronary-artery disease. The Bantu does suffer from coronary atherosclerosis and his myocardium also suffers. For example, in hypertension (a very common disease in the Bantu) Becker [11] stated " the coronary vessels are frequently diseased and the myocardium is frequently gravely damaged ". And Higginson and Pepler [15], comparing Bantu with Americans and Danes, stated " our observations suggest that severe atherosclerosis of the aorta and coronary arteries are less frequent in the hospitalised Bantu of Witwatersrand than among the American and Danish hospital patients *but the differences are not conclusive* " (our italics).

Edendale Hospital, Pietermaritzburg, Natal.

J. D. WOODS
W. LAURIE.

HAZARDS OF CHLOROTHIAZIDE THERAPY

SIR,—I was glad to see the letter by Professor Rosenheim and Dr. Ross (July 26) in which they drew attention to hazards of chlorothiazide (' Saluric ') therapy.

In common with others I have often found that chlorothiazide leads to an increased loss of potassium in the urine, and the danger of a cellular deficiency of potassium developing in patients who are receiving this drug is therefore very real. As is well established such depleted tissues function less efficiently. In particular impaired renal function may ensue and digitalis is less well tolerated and a therapeutic dose may also be a toxic dose: a potassium-depleted myocardium moreover is subject to arrhythmias. Thus the maintenance of adequate digitalisation becomes more difficult and as a consequence the heart-failure may worsen.[16 17]

The serum level of potassium is unreliable as an index of body content [18–20]; normal or even raised levels may occur in the presence of cell deficiency. Moreover, whilst it appears very likely that a low level does nevertheless indicate a cell shortage, in our experience such levels are not often found in congestive cardiac failure. In a series of over 450 patients in congestive cardiac failure, under the care of Dr. O. Brenner, that I studied, lowering of serum-potassium was rare. These patients were receiving diuretics other than chlorothiazide, but to date our experience with chlorothiazide is identical. It is likely that when the serum level of potassium is low, the cellular shortage is very profound.

However, I would like to reinforce their emphasis—namely, that potassium depletion cannot easily, if at all, be diagnosed in the outpatient department let alone in general practice. The diagnosis cannot be made on clinical grounds, nor are there simple tests that may be performed to assess its presence.

It is, therefore, necessary routinely to supplement with potassium the diet of every patient having chlorothiazide. A supplement of about 60 mEq. per day is adequate. But potassium salts are unpleasant to take and may occasion nausea, vomiting, &c.[21] This must be appreciated since there is a real possibility of patients discontinuing their supplements unknown to the doctor. It is helpful, in this connection, to see which of the many salts of potassium that may be given are most acceptable to each patient. I have used potassium chloride, potassium bicarbonate, potassium dihydrogen phosphate, dipotassium hydrogen phosphate, potassium citrate, and potassium effervescens.* Other salts have been used in hospital practice, but cannot be obtained easily in general practice. These salts are best taken in solution and the tablets of potassium effervescens may be dissolved in water. I have found it helpful to give potassium chloride in concentrated grapefruit juice. The amount of each of these supplements to contain approximately 60 mEq. of potassium is as follows:

Potassium supplement	*Amount containing 60 mEq. K (approx)*
Potassium chloride	4·2 g.
Potassium bicarbonate	6·6 g.
Potassium dihydrogen phosphate	8·2 g.
Dipotassium hydrogen phosphate	5·2 g.
Potassium citrate	6·5 g.
Potassium effervescens †	22 tablets

Department of Experimental Medicine, Cambridge, and Queen Elizabeth Hospital, Birmingham.

C. T. G. FLEAR.

DIASTOLIC PRESSURE AND MALIGNANT HYPERTENSION

SIR,—In his letter of July 26 Dr. Cruz-Coke maintains that by measuring diastolic blood-pressure levels against a standard scale, adjusted for age and sex, it is " possible to identify patients with malignant hypertension before changes are evident in the fundus and before left ventricular hypertrophy develops. It also allows the significance of high blood-pressure to be assessed in old people ".

These are large claims. If we could learn to pick out in advance those patients in whom hypertension will sooner or later go to the bad, in consequence of fatal or disabling vascular damage, we could then treat them with the new autonomic paralysing drugs in the assurance that we should be doing much to avert their destined fate.

Unfortunately the criteria suggested by Dr. Cruz-Coke are not enough. We all know that raised arterial pressure in a young man presents a threat much more serious than the same pressure in an old lady. But we still can foretell very little of individual fortune among the members of parallel groups. We know, for example, that out of 10 fifty-year-old men with diastolic pressures of 130 mm. Hg 2 or 3 will probably be dead in a year or so of strokes, heart-failure, or malignant renal change. But we do not know which 3. Another 2 or 3 may very well survive into old age. Again we are unable to identify the lucky ones. And Dr. Cruz-Coke's tables cannot help us.

Nevertheless we can bear in mind some points that will enable us to make a rough selection. This, in fact, is what we do, almost subconsciously, when we first assess a new patient with hypertension. Together with age and sex we certainly consider also the factors of heredity, lability of pressure, and the trend over a period adopted by its resting level, with a

12. Walker, A. R. P. *Brit. med. J.* 1958, i, 1060.
13. *Lancet*, 1958, i, 231.
14. *ibid.* 1957, i, 1091.
15. Higginson, J., Pepler, W. J. *J. clin. Invest.* 1954, **33**, 1366.
16. Fletcher, E., Brennan, C. F. *Brit. Heart J.* 1958, **20**, 204.
17. Lown, B., Levine, S. A. Current Concepts in Digitalis Therapy. London, 1955.
18. Moore, F. D., Edelman, I. S., Olney, J. M., James, A. H., Brooks, L., Wilson, G. M. *Metabolism*, 1954, **3**, 334.
19. Burrows, B. A., Ross, J. F. *Boston med. Quart.* 1956, **7**, 54.
20. Flear, C. T. G., Cooke, W. T., Quinton, A. *Lancet*, 1957, i, 548.
21. Flear, C. T. G., Hill, M., Thomas, G. *ibid.* 1950, i, 1190.

* Now listed in Martindale's *Extra Pharmacopœia*.

† Potassium bicarbonate 26·56; Tartaric acid 16·87; Citric acid 11·25; Sucrose 9·40 } g. per 100 tablets
Granulated on a hot plate.

further thought, probably, for the patient's employment and temperament. Finally we know that the nephritic hypertensives do worst of all.

To seek some arbitrary standard to mark the start of the malignant phase is to betray a total misconception. The malignant phase bears no direct relationship with the pressure itself. A diastolic reading of 110 may be accompanied by a malignant fundus in an eclamptic young woman, while in a man of sixty a diastolic level of 150 may have produced only the earliest retinal changes.

In short, the recognition of individual prognosis amongst hypertensive patients offers one of the supreme clinical challenges of the day. We would do well to confess, however, that as yet the power to make this vital discrimination still largely eludes us.

Victoria Hospital, Blackpool. I. McD. G. STEWART.

ASPIRIN AND PEPTIC ULCER

SIR,—We are interested in the conclusion of Dr. Flint and Dr. Allibone (July 2) that aspirin, "although a gastric irritant, is a rare cause of hæmatemesis".

Since September, 1957, 40 cases of hæmatemesis or melæna were admitted to the Burnley General Hospital. Each patient was questioned carefully concerning drugs taken during the week preceding the bleeding episode. Close questioning was required since many patients habitually take proprietary analgesic preparations and are unaware of an aspirin content of some of these. A history of aspirin ingestion within 48 hours of the bleeding was obtained in 20 cases (50%).

During the months of September, October, and November, 1957, when the influenza epidemic afflicted the community with great severity, 16 cases of hæmatemesis or melæna were admitted to this Hospital. In the corresponding periods in 1952, 1953, 1954, and 1955, the numbers were 11, 16, 14, and 14 respectively. Since a number of medical beds were not in use in 1956 figures for this year are excluded. At the time of the epidemic the considerable publicity in the newspapers and on television advocating aspirin-containing preparations for the relief of influenza, probably resulted in a much greater consumption of aspirin than is usual at this time of year.

If aspirin is to be incriminated in the production of frank gastrointestinal bleeding, one would have expected a significant increase in the incidence of hæmatemesis and melæna during the epidemic months. The figures for 1957 probably represent the true incidence of hæmatemesis and melæna in this area, since the general practitioners would be more than ever likely to regard acute gastrointestinal hæmorrhage as an indication for urgent admission to hospital in view of their very heavy commitments. Our experience would lend support to the conclusions of Dr. Flint and Dr. Allibone.

Burnley General Hospital, Burnley. R. E. FORGIE
J. SHAFAR.

WORDS AND THINGS

SIR,—When I was asked whether I had written your admirable leading article on Another Renal Symposium (Aug. 2, p. 247) I replied with Wilde, "I wish I'd said that," and Whistler, it is well remembered, replied, "Oh, but you will, Oscar."

Your article eloquently concludes "it is not yet certain whether some of the concepts expressed will turn out to be words ('the daughters of earth') or things—'the sons of heaven' in the round Johnsonian phrase."

The quotation is from the preface to the English Dictionary:

"I am not yet so lost in lexicography as to forget that *words are the daughters of earth, and that things are the sons of heaven.* Language is only the instrument of science, and words are but the signs of ideas: I wish, however, that the instrument might be less apt to decay, and that signs might be permanent; like the things which they denote."

Johnson himself was quoting, and apparently incorrectly, for Samuel Madden (1687–1765) wrote in *Boulter's Monument*, L. 377: "Words are men's daughters, but God's sons are things."

I am grateful to you, Sir, for sending me back to Johnson's Preface of which Boswell wrote, "I believe there are few prose compositions in the English language that are read with more delight."

Derby. DOUGLAS HUBBLE.

N.H.S. STAFF COLLEGE

SIR,—Permit me to thank those correspondents who have replied to my letter either privately or in your columns.

I ought to have emphasised that the college would be a meeting place for doctors and their colleagues in the service to talk about people. There is no suggestion that administrators would meet administrators and talk about administration. Too many exclusive coteries have already been created. A new start is proposed to avoid any idea that any one section of our profession or of our lay colleagues is trying to steal a march on the rest.

Brighton. W. S. PARKER.
Medical Officer of Health.

HOOKWORM AND ANÆMIA

SIR,—May we make some comments on the conclusions of Dr. Meiklejohn and Dr. Passmore [1] ("... we suggest that a properly financed research project into the association between hookworm and anæmia is now overdue")?

The view [2–5] that there is seldom a relation between the degree of infestation and the frequency of anæmia in a population was restated in your columns by Foy and Kondi [6] and Trowell [7] on the basis of their experience in India and in Uganda. But in particular local situations of infestation, of temperature, and of humidity [8] hookworm infestation is almost constantly associated with severe anæmia; and there is also clinical and experimental evidence that the *Ancylostoma duodenale* first described by Dubini [9] in Milan in 1843 can give rise to a well-defined type of anæmia.

So we agree with Foy and Kondi [6 10] that "... although hookworm may play a part in the genesis of the tropical microcytic anæmias, this is probably not a paramount one" because certainly not all the microcytic anæmias of tropical countries may be referred to *A. duodenale*, or better to the worm by itself. We also agree with Roche [11] that "the role of hookworm in the genesis of some tropical anæmias is probably a paramount one".

A basis for agreement may be found in the proposition that some at least of the tropical microcytic anæmias are primarily due to hookworm infestation.

Why does *A. duodenale* only exceptionally exert its power to produce anæmia? Recent work on pathogenesis [4 12–14] indicates that deficiency of iron is an essential factor in the production of anæmia. Anæmia appears only when the hookworm is able to induce a severe iron deficiency, either by itself or with the help of other influences. Without sideropenia, and whatever the degree of infestation, no anæmia develops.

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What are the morphological and biochemical characters of anæmia induced by hookworm? Hookworm produces a typical iron-deficiency anæmia. In this conclusion we agree with all who have studied the disease in Italy [15–19] or in other countries (Jugoslavia,[20] France,[21] Portugal,[22] Egypt,[23] Guadalupe,[24] Japan,[25] Brazil.[4 26] Of course when other factors are present—either internal (deficiency in production of intrinsic factor, changes in intestinal bacterial flora, production of infection or infestation, hepatosplenic abnormalities, &c.) or external (deficiencies in B^{12} and folic acid in the diet)—the anæmia may differ from pure iron-deficiency anæmia. Though such associations are common in tropical countries, they are exceptional in Europe where ancylostome anæmia is usually of classical iron-deficiency type.

Our study of more than 100 anæmic patients brought out these features of hookworm anæmia:

(1) Microcytic hypochromic anæmia with red hyperplasia of the bone-marrow caused by inhibition of maturation in the erythropoietic tissue.[12 14]

(2) Hyposideræmia (serum-iron under 50 μg. per 100 ml.) [12 13] hypertransferrinæmia (plasma-transferrin above 350 μg. per 100 ml. [25 27]), and hyperprotoporphyrinoglobulia (free-erythrocyte-protoporphyrin-9 above 100 μg. per 100 ml).[12 25 29]

(3) Intravenous ^{59}Fe is distributed in the typical "iron-deficiency pattern." [14 29]

(4) Constant and quick response to iron therapy.[12 14]

Our investigations into other possible ways in which anæmia could be produced, such as excess hæmolysis, or bone-marrow inhibition by hookworm toxins, have clearly shown that hookworm anæmia [12 14] is not determined in any of these ways.

The correction of the anæmia by the simple administration of iron, while infestation is still present, is the chief evidence that the anæmia depends exclusively on iron deficiency.

The most important question is how the hookworm induces iron deficiency. Hookworm may impair the normal gastro-duodenal processes by which food iron is dissolved and ionised.[14 29] It may also interfere with iron absorption by the duodenal and jejunal mucosa.[14 29] *A. duodenale* also increases the elimination of iron from the gut by bleeding from mucosal lesions. Basing our opinion on our experience with the radioactive method of Gerritsen et al.[31] we believe that, though hæmorrhage, and consequent loss of iron is very important in the genesis of the sideropenia, hæmorrhage cannot by itself explain all the anæmias in those infested by parasites. Severe anæmia may develop in patients with slight blood-loss, and some men with ancylostomiasis may lose about 10–20 ml. of blood a day without becoming anæmic.

The effect of hookworm may be enhanced by a diet extremely poor in iron or by a diet abnormal in calcium and phosphorus content. Such an alimentary factor is of very little significance in Italy and probably in other European countries. In other parts of the world, however, [4 32] it is of fundamental importance in the production of iron deficiency. The size of iron stores is also relevant, and the exhaustion of these reserves, the first step in the development of anæmia is obviously more easily accomplished in patients with initially low reserves.

It is usually a combination of these factors, and not one alone, that explains the development of anæmia in ancylostomiasis. We conclude that hookworm anæmia is a real well-defined clinical entity due to iron deficiency induced by worm infestation.

Department of Medical Pathology,
University of Cagliari,
Italy.

PAOLO LARIZZA
SANDRO VENTURA.

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SHOULD BIBLIOGRAPHIES GIVE TITLES OF PAPERS?

SIR,—Mr. Patey (July 19) has expressed what is a growing concern at the wilfulness of British publishers in not allowing their contributors to provide the title of papers in their references. In your own case, the argument is perfectly valid—they would replace a short article. In other journals, and in many English books, the same practice prevails even when half a page is left blank at the end of an article or a chapter.

Now that "the English literature" enjoys a prestige as great as that of "Eng. Lit." it is surely mandatory that it should be given a final veneer of completeness. I suggest, therefore, that *The Lancet* makes the gesture—how I cannot suggest. Pressed as you are for space, it is a question of quality versus quantity.

Department of Pathology,
Jackson Memorial Hospital,
Miami, Florida.

MAX MILLARD.

REAPPEARANCE OF TABOPARESIS

SIR,—I have just returned from a two months' guest lectureship in Munich, and I can confirm Dr. Noel Harris' remarks (Aug. 9) from my observations at the Universitaets-Nervenklinik. At least four recent cases of general paresis of the insane were admitted during my presence. Syphilis of the central nervous system had apparently not become as rare in the large German cities as it was here, but the recent increase in patients suffering from taboparesis has been noticeable. It was thought to be due to the turmoil and strife of populations in Europe after the late war when treatment of venereal disease was inadequate or lacking.

Department of Experimental Psychiatry,
The Medical School,
Birmingham.

W. MAYER-GROSS.

NEUROLOGICAL COMPLICATIONS OF ASIAN INFLUENZA

SIR,—In your issue of July 5 you published four interesting papers dealing with the neuropsychiatric complications of Asian influenza. In your accompanying annotation you state that psychotic outbursts related to influenza "are a symptom of encephalitis and do not represent a latent psychosis which has been revealed by a generalised infection".

Following the epidemic of Asian influenza in Israel during November and December, 1957, 4 patients who developed psychotic manifestations during the course of the influenzal illness were admitted to Talbieh Psychiatric Hospital, Jerusalem. The psychosis appeared in 3 of the cases within three days of the onset of the influenza. The correlation between the development of the psychosis and recent infection was ascertained by a progressive rise in titre of the hæmoagglutination inhibition for the Asian virus variety during the psychotic outburst. (A detailed report of our cases was recently published in *Dapim Refuim*, Israel, 1958.)

We should like to draw attention to the following features:

(1) Without exception the psychotic reactions occurred in a labile premorbid personality with strong emotional conflicts preceding the onset of the psychosis. In 2 of the cases physical exhaustion was also present.

(2) Physical and neurological examinations including lumbar puncture did not reveal any abnormalities. Repeated electroencephalography gave a normal record in 3 patients. The tracings of the 4th were abnormal, but inconclusive. Therefore, we failed to demonstrate clinical or electroencephalographic evidence of a correlation between the acute psychosis and a presumptive encephalitis.

(3) 3 of the 4 patients were young people under 17. The clinical picture was characterised by a confusional state with psychomotor restlessness, delusions, visual hallucinations, and aggressiveness. The acute psychotic symptoms cleared spontaneously on the average within two weeks. A short-term relapse of the psychotic incident was observed in a single case whose final outcome was also favourable.

(4) On the psychodiagnostic level all patients were found to be of normal intelligence with clear evidence of a disturbance of mental equilibrium. No support could be found for the assumption of structural damage to the brain, nor of an acute manifestation of a latent psychosis, with the illness in the role of a trigger. Rather do we incline to interpret the psychotic episode as the reaction of a personality lacking full integration, maturity, and flexibility to the disturbance of somatopsychic homœostasis caused by the attack of influenza.

A. A. WEISS
M. KAFFMAN
H. Z. WINNIK.

Talbieh Psychiatric Hospital, Jerusalem.

NO MORE NEOLOGISMS?

SIR,—Why not "No More New Words?"?

Chesham, Bucks. FFRANGCON ROBERTS.

SIR,—In reply to the letters by Dr. Pappworth and myself (July 26) you rightly emphasise that an editor has a duty to his contributors, and thus you justify the use of new words which we think are often unnecessary and nearly always serve to obscure. But, Sir, has not an editor a duty to his readers, and is it not important that the reader should understand what the writer is trying to say? If the reader cannot understand, why should the author bother to write, or the journal to print, the paper?

You allude to the centenary of the hypothesis of natural selection. If I remember rightly, the key to that hypothesis was the elimination of the unfit. In this context the unfit are words, and our plea is that the unfit should be eliminated by editorial action.

Oxford. GEORGE PICKERING.

"EXPERIENCE AND INCENTIVE" AWARDS?

SIR,—I have read Dr. Evans' letter last week with interest; but I would like to suggest a more practical basis for administering awards for meritorious work in general practice.

The doctor would apply to the awarding authorities in confidence, giving specified credentials such as 7 to 8 years in general practice (at least 5 as a principal) and a National Health Service list above an accepted minimum varying with districts. The censors would then visit him (one hopes unexpectedly) and inspect; they would demand a definite standard of work, surgery premises, equipment, organisation, and note-taking. Another censor would sit in during a surgery (this time by arrangement); a third would go on visits with him; and yet another (one hopes over coffee) sound him out to see that his basic medicine is still intact, and that he has made attempts to keep up to date. If there is a doctor able to stand up to all this, then he is worthy of the encouragement of an award; and even our most modest colleagues might come forward if they knew that their recognition would in honour bound be kept silent.

Who would our censors be? Presumably they would be chosen from our most capable practitioners, stiffened by consultants with examining experience. It would be understood that our regional examiners would never examine within their own areas.

There is one plea I would put forward, and that is that if a doctor fail to reach the required standard he should be told why, and permitted to reapply after a suitable interval without prejudice.

London, S.E.3. L. I. NORMAN.

CONGENITAL FIBROELASTOSIS OF THE ENDOCARDIUM, NUTRITIONAL HEART-DISEASE, AND MYOCARDIOPATHY OF UNKNOWN ORIGIN

SIR,—Johnson [1] suggested that congenital endocardial fibroelastosis is caused by anoxia of the endocardium. One mechanism by which this may occur is premature closure of the foramen ovale which prevents blood circulating through the left side of the heart in utero. Since the endocardium derives its blood-supply from the blood within the heart chamber it is the site that is predominantly affected. It would seem reasonable to consider, therefore, whether anoxia could play any part in the production of endocardial fibrosis of adults.

One way in which this could occur would be stagnation anoxia of the blood within the heart chambers. It is characteristic of so-called nutritional hearts that they are markedly dilated and pulsate so poorly that they resemble pericardial effusions. In such a quiet heart stagnation of blood might well be expected to occur. Furthermore, one would expect the site most severely affected to be the apex of the ventricle, and this is where the earliest signs of fibroelastosis are usually found.

Two investigations would help to clarify the part played by such a mechanism. Retrograde aortic catheterisation could compare the oxygen saturation levels of blood samples taken from the aorta and from the region of the apex of the left ventricle. Angiocardiography could demonstrate incomplete emptying of the heart in systole, and how long the opaque material stagnates within the ventricles.

It could be contended that all dilated hearts should show a similar change. This is not necessarily so, because cardiomegaly from other causes is not usually associated with the quiet almost motionless heart seen in nutritional heart-disease and myocardiopathy of unknown origin. Active contractions, even if not associated with complete emptying of the heart chamber in systole, may be enough to maintain a turbulence that prevents a layer of stagnant blood forming over the endocardium.

If stagnation anoxia is a significant factor then fibroelastosis and thrombosis become secondary changes. The primary disturbance would be cardiac dilatation, the cause of which remains obscure. Such an explanation would serve to bring these myocardiopathies into much

1. *Arch. Path.* 1952, **54**, 237.

closer alignment and explain why in some cases there is neither fibrosis nor thrombosis.

Furthermore, support for some common factor may be found in Bedford and Konstam's [2] account of the postmortem findings in adult Africans dying of heart-failure of unknown ætiology. Of 17 of these cases 3 had hypoplasia of the aorta, which is known to be associated with congenital fibroelastosis of the endocardium.

Department of Pædiatrics,
Groote Schuur Hospital,
Cape Town. P. M. SMYTHE.

INTRADERMAL TESTS FOR SERUM SENSITIVITY

SIR,—We are in full agreement with Dr. Tasman and his associates [3] regarding the superiority of the intravenous route over the intramuscular in the antitoxin treatment of diphtheria, but we do think that it is an exaggeration of good therapy to advocate that route for all cases however mild and even for all suspected cases.

We differ entirely from them, however, regarding the value of intradermal reactions of any kind as a means of detecting general sensitivity to serum. They quote our article [4] of 1957, but do not mention a previous one [5] dealing with the subject generally and not only in connection with tetanus antitoxin administration. We would refer them to that article.

We both know of instances of severe allergic shock, some of them fatal, which have occurred following antitoxic serum given either intramuscularly or intravenously on the strength of a negative skin test. On the other hand, one of us (L. J. M. L.) has had experience (in the course of titration of scarlatinal antitoxin on scarlet fever patients) of more than 50 cases, with strongly positive intradermal reactions to serum in a dilution of 1 in 10, but no general reactions whatsoever when given a full dose of scarlatinal antitoxin intramuscularly a few hours later. Moreover, many of these patients still had positive skin tests when there could be no more question of general sensitivity remaining. We have come to the conclusion—and many of our colleagues in various hospitals have, too—*that skin sensitivity and general sensitivity do not run parallel.*

Since skin tests have proved so unreliable, we have used and recommended for years the method of a small trial dose of 0·2 ml. of undiluted or diluted serum given subcutaneously for the purpose of detecting *general* sensitivity. This method may, on rare occasions, cause allergic shock in hypersensitive patients, but owing to the small dose and the slow absorption this shock can be quickly controlled.

Hither Green Hospital,
London, S.E.13. L. J. M. LAURENT.

Wellcome Research Laboratories,
Beckenham, Kent. H. J. PARISH.

ANNUAL MEETING OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

SIR,—I am grateful to you for allowing me to use this opportunity of bringing to the notice of the profession that the College is holding its annual meeting this year on Sept. 26 and 27 in Cardiff.

As you know, the College has recently adopted the policy of holding meetings from time to time in provincial centres, and the first of these was held in Manchester in 1955. The purpose of the council in holding these meetings is to bring the College closer to its provincial Fellows and Members and to enable them to take part in some of its activities. The council is particularly anxious that Members of the College shall join us at this meeting, and any other diplomates will of course be very welcome. Fellows have already been notified individually.

The meeting will consist of a reception at Cardiff Castle, kindly given by the Lord Mayor and Council of Cardiff, and a subscription dinner, both on Friday, Sept. 26. Tickets for the dinner (two guineas each) and invitations for the reception can be obtained from the Secretary of the College, but the numbers for both events are limited and early application is necessary.

On Saturday, Sept. 27, the morning will be devoted to scientific exhibitions and surgical operations arranged by the local committee at the Cardiff Royal Infirmary, followed by a fork lunch, kindly given by the Board of Governors of the United Cardiff Hospitals.

In the afternoon, at 2.30 P.M., the statutory annual meeting of Fellows and Members will be held in the Reardon Smith Hall, and this will be followed by the conferment of the Honorary Fellowship of the College on Sir Russell Brain, Bt., who will afterwards deliver a lecture on The Cervical Spine.

The council hopes that this meeting will prove to be as successful an event as was the meeting in Manchester, and we trust that our colleagues in Wales will make a special effort to attend.

Royal College of Surgeons of England,
London, W.C.2. J. PATERSON ROSS.

Obituary

JOHN BROCK BISHOP

M.A., B.M. Oxon., T.D.

Dr. J. B. Bishop, deputy superintendent of Broadmoor Institution, died at his home on Broadmoor Estate on Aug. 4, at the age of 50.

He was a scholar at the Merchant Taylors' School and later an exhibitioner at St. John's College, Oxford, where he took his preclinical course, gaining second-class honours in physiology. His clinical work was done at St. Thomas's Hospital, London, and after qualifying in 1931 he served there as casualty officer and house-physician. Later he was a clinical assistant at the West End Hospital for Nervous Disorders and house-physician at the Victoria Hospital for Children. Until 1939 he was in private practice in Chelsea. During the late war he served in the R.A.M.C. both at home and overseas in North Africa and Italy. He was mentioned in despatches and received the Territorial Decoration with there bars. After the war he continued to serve in a hospital ship. He remained a keen member of the Territorials until his transfer to the Army Emergency Reserve. He went to his last camp only a few weeks ago.

In 1948 he joined the staff of Broadmoor, where he worked first as a medical officer and later as deputy superintendent. From the outset he regarded this as his life's work. Of these years V. G. S. writes:

"Brock Bishop's main interest professionally was not in the science but in the art of medicine and its social applications. The organisation at Broadmoor gave him wide scope for his particular type of work, and his practical common sense was an invaluable asset in such an institution. For two years he sustained practically the whole administration of the institution during the illness of the late Dr. S. G. James, then medical superintendent.

"For some years he was handicapped by a neurological condition which with his characteristic tenacity he forbade

2. Bedford, D. E., Konstam, G.L.S. *Brit. Heart J.* 1946, **8**, 236.
3. Tasman, A., Minkenhof, J. E., Vink, H. H., Brandwijk, A. C., Smith, L. *Lancet*, 1958, i, 1299.
4. Parish, H. J., Laurent, L. J. M., Moynihan, N. H. *Brit. med. J.* 1957, i, 639.
5. Laurent, L. J. M., Parish, H. J. *ibid.* 1952, i, 1294.

to interfere with his everyday life and work. His cheerily shouted 'hullo' used to echo round the blocks as he made his daily visits. Only a week before his death he attended the staff club's horticultural show and made one of those speeches which were always so apt and for which he had a justified reputation. Staff and patients alike have lost a real friend.

"For the last twelve months of his life he held the posts of master of the Worshipful Company of Girdlers and renter warden of the Worshipful Company of Inn Holders. The former office was held by his late father thirty years earlier. He was unmarried, and in all his work he enjoyed the active interest and support of his mother."

WILLIAM HENRY CASSWELL SPOONER

M.B. Lond.

Dr. W. H. C. Spooner, of Blandford, Dorset, was drowned at Brest on Aug. 1 when his yacht *Remarie* was rammed and sunk at her moorings by a tug. His wife and three children, who had joined him a few hours earlier, escaped.

He was educated at Epsom College and qualified from St. Mary's Hospital in 1932. After holding house-appointments at St. Mary's and at St. James' Hospital, Balham, and an assistantship in North Wales, he went into practice at Blandford, where his greatgrandfather, grandfather, and father had practised before him. During the late war he served in the Royal Air Force.

R. Mac K. writes:

"Spooner was very modest about himself but he was a very good doctor indeed. He looked forward all the year to his summer holiday; for the last ten years he took his family cruising in *Remarie* on the Brittany coast. 'Skip' was a good navigator and knew the coast well. Often his was the only yacht among the fishing boats in the anchorage. Last week when, after a week with two companions, he reached Abervrach, he said he was happy to be back on this coast. He was a good painter in water colours and oils and played a great part in the Forum Club at which professional and amateur artists of Dorset met at Blandford. He was an excellent host. Conservative in his outlook, he was open-minded and could admire the Teddy boys for the originality of their dress. Perhaps this was just an illustration of his most thoughtful and courteous way with every one of us. He will be very much missed and not only in Dorset."

A memorial service for Sir Arnold Stott will be held in Westminster Hospital's Chapel at noon on Thursday, Sept. 25.

Appointments

BALLANTYNE, J. C., F.R.C.S., D.L.O.: E.N.T. surgeon, Royal Free Hospital, London.

CONNOLLY, R. C., F.R.C.S.: neurosurgeon, accident unit, Royal National Orthopædic Hospital, Stanmore.

ORTON, PEGGY K. L., F.R.C.S., D.L.O.: E.N.T. surgeon, Elizabeth Garrett Anderson Hospital, London.

PINKER, G. D., M.B. Lond., F.R.C.S.E., M.R.C.O.G.: consultant obstetrician and gynæcologist, Samaritan Hospital and St. Mary's Hospital, London.

SPENCER, RALPH, M.B. Manc., F.R.C.S.E.: assistant radiotherapist, Liverpool Radium Institute.

VAN WIJK, P. J., M.B. W'srand: radiological registrar, Papworth and Addenbrooke's Hospitals, Cambridge.

WEMYSS, CAMERON, M.B. Edin., D.P.H.: group medical superintendent, Victoria Hospitals, Glasgow.

Manchester Regional Hospital Board:

GUYER, O. K. G., M.D. Edin., M.R.C.P.E.: consultant geriatrician, Preston and Chorley group of hospitals.

LEES, V. T., M.B. Manc., D.O.M.S.: consultant ophthalmologist, Wigan and Leigh group of hospitals.

POPHAM, R. D., M.B. Lond.: consultant pathologist, Bury and Rossendale group of hospitals.

WADE, E. G., M.D. Manc., M.R.C.P.: consultant cardiologist, jointly with the United Manchester Hospitals.

Notes and News

ACCIDENTS TO CHILDREN

ACCIDENTS have now become the leading cause of death among children both in the United States and in Europe. At a seminar held at Spa last month by the World Health Organisation it was pointed out that children must not be overprotected, and should be taught to cope with dangerous situations; but at the same time unnecessary dangers should be removed.

In different countries the prevailing risks differ. Drowning is particularly frequent in Scandinavia, the Netherlands, and France. In Spain, small children lose their lives or are seriously injured by falling into open braziers—a danger that is gradually disappearing as housing is modernised. "A similar problem exists in the British Isles, where the open fireplace is the usual way of heating the home." In Italy and Poland, damage from explosives left from the last war is a prominent hazard, which vigorous propaganda has done much to reduce. Poisoning of young children is common in the U.S.A., Switzerland, and Sweden—countries where many chemicals are to be found in the home. Suffocation of small children who, while playing, put their head into a plastic bag is reported as a real danger in France, Belgium, Denmark, and Sweden.

"Small children do not understand dangers and must be protected from them, particularly from life-threatening hazards, but as they grow older they must be taught to cope with dangerous situations. They must learn to climb, to jump and to fall, to handle knives, forks and scissors, to swim, to use matches and understand fire, to get along in traffic. The wise parent will thus protect the child as far as ever possible from dangers from which the child can learn nothing and not worry about small accidents from which the child can learn how to avoid them. It is through this positive approach combined with the elimination of deadly hazards from the environment of the child that it will be possible to reduce the number of accidents."

ROYAL MEDICAL BENEVOLENT FUND

DURING 1957 this Fund disbursed £43,942 in grants and annuities. The number of cases (398) helped by grants was almost the same as in the previous year, but the grants rose by £2599. Though the number of annuitants decreased by 6, annuities amounting to £12,406 (£455 more than in 1956) were distributed. "This increase in the amount of grants and annuities to approximately the same number of beneficiaries appears to reflect the rise in the cost of living, and the Rent Act, of course, has made its expected impact. This may well become more pronounced in 1958." The number of people who benefit is much larger than the number of cases quoted. Many of these include married couples, children requiring sustenance and education, and widows with families.

In his report for the committee of management, Dr. T. Anwyl-Davies, the hon. secretary, asks for more help in meeting demands which, in spite of the Welfare State, are ever expanding.

"To increase our income, new subscribers are essential. We are very grateful to those who subscribe annually and we appeal to them to suggest to their colleagues that they might wish to do likewise . . . Surprisingly enough, many of the profession do not know of its existence or of its work. Many gladly subscribe when their attention is drawn to its purpose of acting as a Good Samaritan to the whole of the medical profession. The Fund gives assistance to distressed members of the profession, their wives, widows and children. Immediate help is given in urgent cases and all deserving applicants are treated impartially."

Dr. Anwyl-Davies appeals to subscribers, new and old "to consider the very profitable and simple procedure of signing seven-year covenants". Some 1275 already subscribe by covenant and last year £5845 was recovered, without further cost to the "covenanted" subscribers, from the Inland Revenue. He also thanks those who remember the Fund in their wills—however small the legacy may be. "Last year the legacies received came to the welcome sum of £29,495, a very valuable addition to the accumulated funds."

The report for 1956 mentioned that under the Giffen bequest a house was to be bought and equipped for indigent doctors. A large

house in Putney is now to be converted into five self-contained flats each consisting of a bedroom, sitting-room, bathroom, and kitchen.

During the year the Ladies' Guild distributed more than £13,000. This auxiliary helps with visiting, the education of children, the care of young widows, and the distribution of medical comforts, gifts of clothing, coal and other necessities. Parcels of clothing, with the donor's name and address inside, should be sent to the clothes room, Ladies' Guild of the R.M.B.F., Tavistock House (North), Tavistock Square, London, W.C.1.

At the annual general meeting on July 30 Sir Henry Tidy was re-elected president, Mr. F. A. Juler hon. treasurer, and Dr. Anwyl Davies hon. secretary. The Fund's address is 1, Balliol House, Manor Fields, Putney, London, S.W.15.

THE BIRMINGHAM DENTAL HOSPITAL

The year 1958 is celebrated for many important centenaries in medicine, including that of this unique hospital—unique because it is the oldest dental institution in this country and possibly in the world.

It was Samuel Adams Parker, a son of Langston Parker, the famous surgeon on the staff of the Queen's Hospital, who founded the Birmingham Dental Dispensary early in 1858 when he had but recently finished his dental studies at the Middlesex Hospital. The first premises were at 13, Temple Street, and it is interesting that the committee set out to undertake not only extractions but also stoppings and scalings as well as "the regulation of children's teeth." C. J. Fox had in 1855 opened a similar dispensary in London, but it was not to last long. The Birmingham Dental Dispensary, on the other hand, prospered and had already moved premises twice before the passing of the Dental Act in 1878. Its more active concern with teaching necessitated in 1882 a third move, this time to 71, New Hall Street. When in 1900 Mason's College became the University of Birmingham, another move was soon required, and in 1905 the hospital occupied its present site which it has more than outgrown. A fifth move, we hope, will not be delayed long.

Mr. R. A. Cohen has gone to great pains in preparing a history of the hospital [1] writing of the many devoted people who have served it so well in this hundred years.

University of Oxford

On Aug. 2 the following degrees were conferred:

D.M.—G. A. Rose.
B.M.—M. A. Pratelli.

Shortage of Staff at York

Owing to shortage of junior staff in the surgical departments of York hospitals, admission to the surgical wards has been restricted (*Yorkshire Post*, July 30). At a meeting of the York "A" and Tadcaster Hospital Management Committee the secretary said there should be five house-surgeons at the city, county, and military hospitals, but in fact there was only one, which was not enough for proper supervision of the wards. The consultant staff had therefore agreed for the time being to admit only emergency cases, urgent cases from the waiting-list, and some minor cases which would not need much supervision. At the York Maternity Hospital, owing to a shortage of nurses, only one ward is being used.

Future Role of the Special Hospitals

When he opened a £100,000 ward block at the Royal Orthopaedic Hospital, at Northfields, near Birmingham, on Aug. 2, Sir Harry Platt said that there was a powerful school of thought whose adherents held that the day of special hospitals was over. This was doubtless true of small special hospitals, situated in isolation and unable to share in the diagnostic facilities of the modern general hospital. He was one who believed that a limited number of large special institutions would be needed for many years to come. But such institutions must "justify their continued existence not only by providing for long-stay patients a comprehensive range of rehabilitation facilities, but must, under the guidance of the university medical schools, become centres of research and teaching".

1. The History of the Birmingham Dental Hospital and Dental School. By R. A. Cohen L.D.S., F.S.A. Published by the Board of Governors of the United Birmingham Hospitals.

Medical Research Council

The Council announce that they have made the following travelling awards for 1958–59:

Rockefeller fellowship in medicine.—Dr. G. Burnstock, research assistant, department of pharmacology, University of Oxford; Mr. P. J. Holloway, external scientific staff member, M.R.C. Laboratories, Hampstead; Mr. W. B. Jennett, lecturer in neurosurgery, University of Manchester; Dr. A. P. Mathias, lecturer in biochemistry, University College, London; Dr. R. P. Michael, clinical research fellow, department of experimental neuroendocrinology, Institute of Psychiatry, Maudsley Hospital, London; Dr. P. H. A. Sneath, scientific staff member, National Institute for Medical Research, Mill Hill, London.

Lederle fellowship in medicine.—Dr. R. J. Linden, lecturer in physiology, University of Leeds.

Alexander Pigott Wernher fellowship in ophthalmology and otology—Dr. G. B. Arden, research assistant, Institute of Ophthalmology, London.

French exchange scholarships in medical science.—Miss J. E. Cremer, scientific staff member, M.R.C., toxicology research unit, Carshalton, Surrey; Miss S. Reiman, assistant lecturer in psychology, Institute of Psychiatry, Maudsley Hospital, London.

The following awards have been made after nomination by the Council:

Lilly fellowships in medicine.—Mr. J. D. Griffiths, senior registrar in surgery, St. Bartholomew's Hospital, London; Dr. C. W. M. Wilson, lecturer in pharmacology and therapeutics, University of Liverpool.

United States Public Health Service, National Institutes of Health, Bethesda, Maryland, fellowships in medical science.—Dr. B. S. Hartley, research fellow, department of biochemistry, University of Cambridge; Dr. K. W. Cross, reader in physiology, St. Mary's Hospital Medical School, London; Dr. A. Doig, medical registrar, Royal Infirmary, Edinburgh.

Social Security Agreement with Yugoslavia

The convention on social security between the United Kingdom and Yugoslavia, which was signed on May 24, has now been ratified and will come into force on Sept. 1. The convention covers cash benefits for unemployment, sickness, maternity, old age, widowhood, orphanhood, industrial accidents and diseases, death, and family allowances.

Licence of Ravensburg Doctor Withdrawn

The Schleswig-Holstein Minister of the Interior has withdrawn the medical licence of Dr. Herta Oberheuser. At the annual representative meeting of the British Medical Association (see *Lancet*, July 19, 1958, p. 148) a resolution was passed expressing distress that a doctor who had been convicted of medical war crimes should be allowed to return to medical practice.

More Psychiatrists for Birmingham

On the recommendation of their consultant services committee Birmingham Regional Hospital Board have agreed to the appointment of 12 additional consultant psychiatrists in the region (*Birmingham Post*, July 24). Subject to the approval of the Ministry of Health, it is intended to fill 3 of the posts immediately. The committee believe that it would be impossible to fill all 12 posts at once.

Dr. P. H. C. Fowell has left the residue of his estate, almost £30,000, to the Imperial Cancer Research Fund.

Surgeon Commander J. Alexander, R.N.V.R., has been awarded the Royal Naval and Royal Marine Forces Volunteer Reserve decoration.

Surgeon Captain W. P. E. McIntyre is to be promoted surgeon rear-admiral in November when he will succeed Surgeon Rear-Admiral R. L. G. Proctor as deputy medical director-general of the Navy.

Dr. J. T. Hayward-Butt has been appointed assistant professor of anæsthesiology at the State University of Iowa.

Dr. M. B. McIlroy has been appointed an associate professor of medicine in the University of California.

The Royal Society has awarded a Mr. and Mrs. John Jaffé donation studentship to Dr. Jennifer Wildy to work on the biosynthesis of the protein and hæm components of hæmoglobin in the department of chemical pathology of University College Hospital Medical School.

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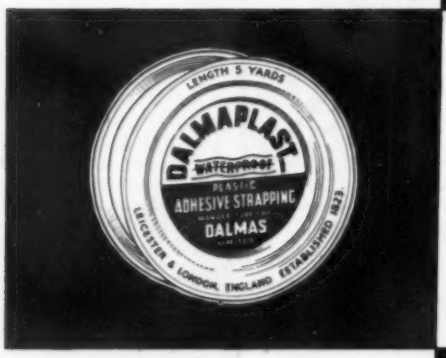

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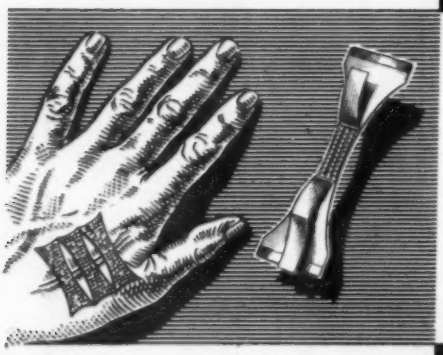

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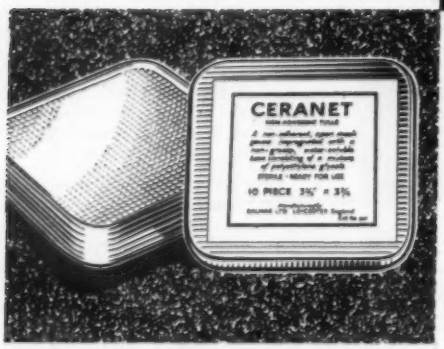

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(1) 'Topical Aspects of Poliomyelitis'; 'Journal of the Royal Society of Health' Dec. 1956.
(2) World Health Organisation Technical Report Series, No. 81, 'Expert Committee on Poliomyelitis'.
(3) Domestos Technical Report D.R. 82A.

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Academic and Educational

EXAMINING BOARD IN ENGLAND

by the

ROYAL COLLEGE OF PHYSICIANS OF LONDON

and the

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Notice is hereby given that the following EXAMINATIONS will commence on the dates stated below:

DIPLOMA IN CHILD HEALTH
17th September

DIPLOMA IN MEDICAL RADIO-DIAGNOSIS
16th October

DIPLOMA IN MEDICAL RADIOTHERAPY
16th October

DIPLOMA IN PATHOLOGY
30th October

Applications and fees for either or both Parts of an Examination must reach the Secretary, Examination Hall, Queen-square, London, W.C.1, at least 21 days before Part I of the Examination begins. FRANCIS M. STENT, Secretary.

UNIVERSITY OF LONDON

BRITISH POSTGRADUATE MEDICAL FEDERATION
INSTITUTE OF NEUROLOGY
(Queen-square)

COURSE FOR CONSULTANTS—"MODERN TRENDS IN NEUROLOGY AND NEUROSURGERY"

A 2-day Course for Consultants in General Medicine and Surgery on "Modern Trends in Neurology and Neurosurgery" will be held at The Institute of Neurology, National Hospital, Queen-square, London, W.C.1, on FRIDAY, 26TH SEPTEMBER and SATURDAY, 27TH SEPTEMBER, 1958. The subjects covered will include methods of investigation, and various aspects of cerebral haemorrhage, Parkinsonism, epilepsy, &c. The fee for the course will be £2 2s. (to include lunch, coffee, and tea).

Details may be obtained from The Dean, to whom application should be made as early as possible before 13th September.

THE ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE

THE DIPLOMA IN PUBLIC HEALTH
THE DIPLOMA IN INDUSTRIAL HEALTH

The next COURSES OF INSTRUCTION for the above Diplomas will commence on 12TH SEPTEMBER, 1958. Tuition may be taken whole-time or part-time.

Prospectuses, enrolment forms, and full details may be obtained from the Dean, 23, Queen-square, London, W.C.1 (Telephone: TERminus 4788/6206).

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY

THE SAVILL ORATION 1958

(in memory of the late Dr. T. D. Savill, Physician to the Hospital) will be delivered by Sir RUSSELL BRAIN, Bart., D.M., F.R.C.P., at the Hospital, 91, Dean-street, London, W.1, on THURSDAY, 16TH OCTOBER, at 8.15 P.M.

Subject: "The Pathogenesis and Treatment of Endocrine Exophthalmos."

Admission by ticket only, for which application should be made to the Hospital Secretary before 1st October, 1958.

UNIVERSITY OF MANCHESTER

A SHORT INTENSIVE COURSE in the Practice of Industrial Medicine will be held in the Department of Occupational Health, Manchester University, commencing MONDAY, 20TH OCTOBER, 1958, to SATURDAY, 25TH OCTOBER, 1958, inclusive. Numbers will be strictly limited. Registration fee £8.

Applications should be sent to the Secretary, Nuffield Department of Occupational Health, Clinical Sciences Building, York-place, Manchester, 13, from whom further particulars may be obtained.

GUY'S HOSPITAL MEDICAL SCHOOL. Applications are invited for the appointment of Whole-time RESEARCH FELLOW in the Cardiac Department of Guy's Hospital, to work primarily on the problems of heart disease with special reference to surgical treatment. The work would include the clinical aspects, and previous clinical experience and a higher qualification would be an advantage. Salary within the range £935–£1210 p.a., according to qualifications and experience. The appointment would be for 1 year commencing not later than 1st October, 1958.

Applications, with the names of 3 referees, should be sent to the Dean, Guy's Hospital Medical School, London Bridge, S.E.1, by 23rd August, 1958.

UNIVERSITY OF LONDON. The Senate invite applications for the CHAIR OF LARYNGOLOGY AND OTOLOGY, tenable at the Institute of Laryngology and Otology. Salary within the range £2500–£3000 a year.

Applications (10 copies) must be received not later than 31st October, 1958, by the Academic Registrar, University of London, Senate House, W.C.1, from whom further particulars may be obtained.

THE UNIVERSITY OF LEEDS. Department of Medicine. Applications are invited for the post of RESEARCH FELLOW. The successful applicant will be expected to undertake research in conjunction with the Professor of Medicine. Applications would be especially welcome from candidates with a special knowledge of experimental techniques in relation to the study of diabetes mellitus. The Fellow will have clinical duties under the supervision of the Professor of Medicine, particularly in relation to diabetes mellitus, and the appointment will carry the honorary status of Registrar or Senior Registrar with the United Leeds Hospitals and the Leeds Regional Hospital Board. Appointment is for 1 year in the first instance, renewable up to 3 years. Salary range will be closely related to that of the comparable grade in the National Health Service.

Applications (3 copies) should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 6th September, 1958.

THE UNIVERSITY OF LEEDS. Department of Pathology. Applications are invited from candidates with a registered medical qualification for appointment as ASSISTANT LECTURER IN PATHOLOGY from 1st November or such other date as may be arranged. Salary on scale £900–£100–£1100 a year, according to age, qualifications and experience. The person appointed will be required to assist in the routine work of the Department of Pathology (which includes the haematology of the General Infirmary at Leeds) but will be expected also to take part in some research.

Applications (3 copies), stating date of birth, qualifications and experience, together with the names of 3 referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 30th September, 1958.

THE BERKELEY FELLOWSHIP

(Founded in memory of the late Sir G. H. A. Comyns Berkeley and his wife, Ethel Rose Berkeley)

The Berkeley Fellowship was founded under the will of the late Sir G. H. A. Comyns Berkeley to provide an opportunity for research in medicine, or for visits to medical institutions or hospitals to a person elected jointly by the Master and Fellows of Gonville and Caius College, Cambridge, and the Council of the Middlesex Hospital Medical School. Under the terms of the bequest, medical centres in any part of the world may be visited, with the exception of Oxford or Cambridge.

Applications from graduates in medicine of the Middlesex Hospital Medical School are invited for the Fellowship. The period of tenure of the Fellowship and the emoluments will depend upon the circumstances of each case. A Fellowship will not normally be awarded for a period shorter than 3 months or longer than 1 year, but applications for renewal will be considered. The emolument may be paid as stipend or as grant to cover travel and other expenses necessarily incurred by the Fellow in the performance of his programme of work, or partly as stipend and partly as grant. The total emolument allowed for the present Fellowship will not exceed £1600 for 12 months.

Applications (6 copies) should reach the Dean of the Middlesex Hospital Medical School by 13th September, 1958, and should include the following information:—

(*a*) Name, address, and age.
(*b*) Qualifications and experience.
(*c*) Present appointment.
(*d*) Programme of work proposed, with estimate of necessary expenses.
(*e*) Other sources of financial assistance, including any stipend from present appointment, if continued during the tenure of the Fellowship.

AUSTRALIA. UNIVERSITY OF SYDNEY. Lectureship/ SENIOR LECTURESHIP IN HISTOLOGY AND EMBRYOLOGY. Applications are invited for the above position. Candidates with a principal interest in morphological, physiological or chemical cytology will be preferred. Salary for a Lecturer is within the range £A1500–£A90–£A2100 p.a.; for a Senior Lecturer £A2200–£A80–£A2550 p.a. In each case cost-of-living adjustment will be allowed. The salary is subject to deductions under the State Superannuation Act. The commencing salary will be fixed according to the qualifications and experience of the successful applicant. Under the staff members' housing scheme in cases approved by the University and its bankers, married men may be assisted by loans to purchase a house.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. The closing date for the receipt of applications, in Australia and London, is 13th September, 1958.

IBADAN, NIGERIA. UNIVERSITY COLLEGE. Applications are invited for SENIOR LECTURESHIP in Department of Preventive and Social Medicine. Initial appointment 3 years. Clinical salary scales £1850–£100–£2450 p.a. Post carries honorary Consultantship to University College Hospital. Passages paid for appointee, wife, and 3 children under 11 years, on appointment, annual overseas leave and termination. Children's, car, and outfit allowances. F.S.S.U. Part-furnished accommodation.

Detailed applications (10 copies), naming 3 referees, by 15th September, 1958, to Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1, from whom further particulars may be obtained.

Hospital Services: Senior Appointments

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Hackney Group of Hospitals

Part-time CONSULTANT in Obstetrics and Gynæcology for 7 sessions a week. Duties mainly at Hackney Hospital, E.9. Residence within reasonable distance of hospital required.

Romford Child Guidance Clinic

Part-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) for 3 sessions a week. Clinic serves Romford and Dagenham.

Tilbury and South East Essex Group of Hospitals

Part-time CONSULTANT PSYCHIATRIST for 2 sessions a week. Duties at Orsett branch of Tilbury and Riverside General Hospital, near Grays.

Applications (5 copies), stating post concerned, and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 13th September, 1958.

ROYAL FREE HOSPITAL, Gray's Inn-road, W.C.1. Applications are invited from registered medical practitioners for the post of Part-time DIRECTOR of Diagnostic Radiology (Consultant grade). Applicants must hold the Diploma in Medical Radiology, and possession also of a higher qualification is desirable.

Applications, giving details of qualifications and experience, together with the names of 3 referees, should be sent to the Secretary to the Board of Governors not later than 6th September, 1958.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(*a*) Whole-time CONSULTANT SURGEON, North Staffordshire Royal Infirmary, Stoke-on-Trent, for duties in large casualty department receiving all casualties from North Staffordshire. Successful applicant will work in conjunction with the orthopedic surgeons and with the surgeon-in-charge of the Burns Unit; 4 notional half-days weekly will be allocated for work in general surgery. This is a new appointment designed to strengthen and coordinate the casualty services; there will be a possibility of a reallocation of duties so that 9 notional half-days are devoted to general surgery at some future date. Higher qualification and wide experience in general and traumatic surgery essential.

(*b*) Whole-time CONSULTANT in Anæsthetics, Birmingham (Selly Oak) Group; duties mainly at Selly Oak Hospital. Wide experience specialty and higher qualifications required.

Applications (15 copies), stating age, qualifications, nationality, present and previous appointments, and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 15th September, 1958.

BRISTOL CLINICAL AREA. South Western Regional HOSPITAL BOARD. Applications are invited for the appointment of a CONSULTANT GENITOURINARY SURGEON in the Bristol Clinical Area. The appointment will be on a maximum part-time (9 sessions) basis. The successful candidate will have charge of beds at Southmead Hospital, Bristol, and will be required to visit other hospitals in the clinical area as determined by the Regional Board.

Applications (12 copies), stating date of birth, qualifications, and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 6th September, 1958.

CROYDON. MAYDAY HOSPITAL. (595 Beds.) Croydon GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum Tenens SURGEON required (whole-time) 25th August–1st September and 8th–18th September.

Applications in writing, with names of 2 referees, to GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon.

LEEDS REGIONAL HOSPITAL BOARD. Applications are invited for appointment of Maximum Part-time CONSULTANT in General Medicine for duties at the Harrogate General and other hospitals in the Harrogate and Ripon Group. Successful candidate will be required to reside in Harrogate and also to devote 2 sessions entirely to Geriatric work. Cardiological experience an advantage.

Applications (12 copies), stating age, qualifications and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park Parade, Harrogate, by 15th September, 1958.

LEEDS REGIONAL HOSPITAL BOARD. Locum ConSULTANT in Ophthalmology (whole-time) for duties in Leeds and Harrogate. The post will be vacant in September and the appointment will be for approximately 3–4 months.

Applications, stating age, qualifications, details of appointments held showing dates, with the names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 30th August, 1958.

LEEDS REGIONAL HOSPITAL BOARD.

Whole-time SENIOR HOSPITAL MEDICAL OFFICER in Anæsthetics, Huddersfield Group. Person appointed to reside in Huddersfield.

Whole-time SENIOR HOSPITAL MEDICAL OFFICER in Pathology, Harrogate. Successful candidate to work under the general guidance of the Consultant in charge of the Department and to reside in Harrogate.

Applications (12 copies), stating age, qualifications and details of appointments held (showing dates), with names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 16th September, 1958.

LEEDS. THE UNITED LEEDS HOSPITALS and THE LEEDS REGIONAL HOSPITAL BOARD. A CONSULTANT ANÆSTHETIST is required for part-time duties in Thoracic and General Surgical Anæsthesia—5 sessions per week at the General Infirmary at Leeds and 4 sessions per week in hospitals under the control of the Leeds Regional Hospital Board. Candidates must have had extensive experience in anæsthesia for thoracic surgery and must hold a higher qualification in anæsthetics.

Applications, stating age, nationality, qualifications, experience (with dates), and giving the names of 3 referees, to be sent to the undersigned by 30th August, 1958.

J. ARNOLD TUNSTALL,
Secretary to the Advisory Appointments Committee.
The General Infirmary, Leeds, 1.

OXFORD REGIONAL HOSPITAL BOARD. Locum RADIOLOGIST (Senior Registrar or Consultant), High Wycombe Area, whole-time or part-time over 4 sessions, for first 2 weeks in September.

Applications, stating qualifications, experience, and naming 2 referees, to Secretary, 43, Banbury-road, Oxford.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR ASSISTANT PSYCHIATRIST required at the Towers Hospital, Leicester. Salary scale £1653 15s.–£52 10s.–£2126 5s. p.a.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 6th September, 1958.

LIVERPOOL REGIONAL HOSPITAL BOARD. Ormskirk GROUP. Applications are invited for the post of Whole-time Locum Tenens ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer) in the above group for 6 months in the first instance.

Forms of application from Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 55, Castle-street, Liverpool, 2, to be returned not later than 30th August, 1958.

VINCENT COLLINGE, Secretary to the Board.

LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for the post of Part-time CONSULTANT ANÆSTHETIST giving 7 notional half-days mainly in the Southport Group with some duties in the North Liverpool Group. Candidates must have had at least 5 years' recognised training and experience in anæsthesia and must be Fellows of the Faculty of Anæsthetists.

Forms of application from Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 55, Castle-street, Liverpool, 2, to be returned not later than 30th August, 1958.

VINCENT COLLINGE, Secretary to the Board.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens ANÆSTHETIST required, West Wales Hospital Management Committee area, from 25th August, 1958, for approximately 6 weeks.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens ASSISTANT PSYCHIATRIST required, Morgannwg Hospital, Bridgend, immediately for approximately 3 months.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens CONSULTANT RADIOLOGIST required Merthyr and Aberdare Hospital Management Committee area immediately, for approximately 3 months.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens required as MEDICAL OFFICER (Senior Hospital Medical Officer) IN CHARGE at Mount Pleasant Hospital, Swansea (general medicine, chronic sick, diseases of the chest, general surgery, obstetrics, &c.).

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

DUBLIN. NATIONAL CHILDREN'S HOSPITAL, 88, Harcourt-street, DUBLIN. PATHOLOGIST required for the above Hospital. Salary £1200 p.a. 6 sessions per week.

Immediate application, with names of 2 referees, to House Governor.

AUSTRALIA. TASMANIA. ROYAL HOBART HOS-PITAL. Applications closing with the General Superintendent on 1st November, 1958, are invited from medical practitioners possessing qualifications registrable with the Medical Council of Tasmania, for the whole-time appointment of PATHOLOGIST. The Royal Hobart Hospital is a general hospital of 530 Beds. Duties involve the responsibility for the conduct of the Hospital Laboratories. Salary £A3000 p.a. Fares to Tasmania can be provided if desired upon certain conditions, or alternatively an assisted passage can be arranged.

Further details and application forms available from the General Superintendent, Royal Hobart Hospital, Hobart.

H. M. WRIGHT, Secretary.

Box 495A, G.P.O., Hobart.

CANADA. UNIVERSITY OF ALBERTA HOSPITAL, EDMONTON, ALBERTA, CANADA. Applications are invited for the position of ASSISTANT DIRECTOR of the Department of Clinical Laboratory Services. The duties will be concerned with the future development of the biochemistry laboratory service in the Hospital, consulting and advising on clinical problems and research projects involving biochemistry and teaching. A teaching appointment in the University of Alberta Medical School, while not automatic with this appointment, is customary. There will be ample opportunity to carry on individual research. The qualifications required are a degree in medicine and special training and experience in biochemistry. Preference will be given to those holding the M.R.C.P. or F.R.C.P., or a doctorate degree in biochemistry. Male, age 30–40, preferred but not essential. Salary $10,000–$12,000 p.a. Further details may be obtained from Professor E. J. King, Postgraduate Medical School, Ducane-road, W.12, London, England.

Interested parties should apply to the Medical Superintendent, University of Alberta Hospital, giving full details and the names of 2 referees.

NEW ZEALAND. WAIKATO HOSPITAL, Hamilton, NEW ZEALAND. Applications are invited from suitably qualified medical practitioners of the British Empire for the position of Full-time ORTHOPÆDIC SURGEON at the above Hospital. Preference will be given to applicants possessing postgraduate degrees. Salary in accordance with the Hospital Employment (Medical Officers) Regulations as either:

(*a*) Senior Registrar £N.Z.1010–£N.Z.1170 plus allowance of £N.Z.200 in lieu of residence, or

(*b*) Junior Specialist £N.Z.1640–£N.Z.1940 (non-resident).

An allowance will be paid on arrival, towards travelling expenses incurred, in travelling to take up appointment.

Conditions of appointment and form of application are available from the Office of the High Commissioner for New Zealand, 415, The Strand, London, W.C.2. Applications close with the Acting Secretary, Waikato Hospital Board, P.O. Box 934, Hamilton, New Zealand, on Thursday, 30th October, 1958.

Hospital Services: Junior Appointments

CHILDREN'S HOSPITAL, Sydenham, S.E.26. Senior RESIDENT MEDICAL OFFICER (Senior House Officer grade) required for 1 year. Duties include medicine and surgery. Recognised for D.C.H. Previous pædiatric experience essential.

Apply, naming 2 referees, to Administrative Officer by 22nd August, 1958.

DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich, S.E.10. HOUSE SURGEON (pre-registration) required immediately.

Applications, stating age, nationality, qualifications and experience, with names of 2 referees, to be sent to the Secretary.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. SENIOR HOUSE OFFICER in the General Medical Department required, with duties mainly in the Geriatric Department, with facilities for higher examination and insight into the working of general practice. Whole-time appointment for 6 months in the first instance from 16th September, 1958.

Applications, with 2 testimonials or names of 2 referees, to the Medical Director by 23rd August, 1958.

GUY'S HOSPITAL, S.E.1. Applications are invited for the post of REGISTRAR (mid-grade) in the Department of Dermatology, with duties from 1st October, 1958, until 30th September, 1959, in the first instance. It is desirable that applicants should be in possession of the M.R.C.P.

Forms of application are obtainable from, and should be lodged with, the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 21st August, 1958.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. RESIDENT HOUSE SURGEON (orthopædics) required 8th October, 1958.

Detailed applications, copies 2 recent testimonials, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 30th August, 1958.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE SURGEON for Gynæcology and General Surgery.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

HORNSEY CENTRAL HOSPITAL, Park-road, N.8. JUNIOR HOSPITAL MEDICAL OFFICER for 1 year in the first instance, renewable annually. Resident post offering wide experience in all branches of medicine. This is a general practitioner hospital of 60 Beds with the necessary Consultant services. The Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, the Group Secretary, 46, Cholmeley Park, N.6 (ARChway 3070, extension 527), by 25th August, 1958.

KING'S COLLEGE HOSPITAL, Denmark Hill, S.E.5. Applications are invited for the post of SENIOR REGISTRAR in Paediatrics, with effect from 1st October, 1958.

Applications, stating age, education, qualifications and experience, and giving the names of 2 referees, should be sent to the undersigned not later than 30th August, 1958.

S. W. BARNES, House Governor.

KING'S COLLEGE HOSPITAL, Denmark Hill, S.E.5. Applications are invited for the appointment of SENIOR RESIDENT MEDICAL OFFICER at the Belgrave Hospital for Children, from 1st October, 1958. The appointment is for 1 year in the first instance and will be in the grade of Registrar.

Applications, stating age, education, qualifications and experience, together with the names of 2 referees, should be sent to the undersigned by 30th August, 1958.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Locum SURGICAL REGISTRAR required for general surgery, orthopædics and E.N.T. work from 23rd September to 23rd October, 1958, in the first instance.

Apply in writing to the Secretary.

LAMBETH HOSPITAL, Brook-drive, S.E.11. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the post of SURGICAL REGISTRAR. The appointment is normally for 2 years, but is subject to review at the end of 1 year. It is recognised for the F.R.C.S. Duties comprise general surgery, orthopædics and E.N.T. The post is resident or non-resident, but if the latter the successful applicant will be required to sleep in on nights on duty.

Forms of application obtainable from the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, by 6th September, 1958.

LEWISHAM GROUP LABORATORY, Lewisham Hospital, London, S.E.13. Applications are invited for 1 of 2 posts of SENIOR HOUSE OFFICER in Pathology. Vacant 30th September. The appointment may be either fully resident or resident only when on duty.

Applications, stating age, qualifications, and experience, with copy testimonials, or names of referees, to the Group Secretary, Lewisham Hospital, S.E.13.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. 2 vacancies (1 resident, 1 non-resident) occur 1st October, 1958, for HOUSE PHYSICIANS. Appointments for 6 months, 4 in London, 2 at the Country Branch, near Letchworth, and post graded as House Officer. Duties include work in the Outpatient Department and Special Clinics as well as in wards. The resident post will be attached to the Cardiological firm during the 4 months in London.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 20th August.

J. ROBBINS, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. A vacancy occurs 1st October, 1958, for RESIDENT SURGICAL OFFICER. Appointment for 6 months, with prospect of renewal. Post graded as Senior House Officer or Registrar, according to qualifications and previous surgical experience.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 recent testimonials, should reach the undersigned not later than 20th August. J. ROBBINS, House Governor.

London Chest Hospital, E.2.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of REGISTRAR in General Medicine becoming vacant in September. A higher qualification, although desirable, is not essential.

Applications (10 copies), giving the names and addresses of 3 referees, should be received by the undersigned by 5th September, 1958. H. BRIERLEY, House Governor.

LONDON HOSPITAL, Whitechapel, E.1, and THE NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR to the Bernhard Baron Institute of Pathology becoming vacant on 1st October, 1958. The appointment will be for 1 year, renewable for a maximum of 4 which includes 1 year to be spent at a hospital within the Region.

Applications (10 copies), giving the names and addresses of 3 referees, should be received by the undersigned by 28th August, 1958. H. BRIERLEY, House Governor.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of SENIOR REGISTRAR or REGISTRAR, according to experience, to the Department of Neurosurgery. The appointment becomes vacant on 1st October, 1958. A higher surgical qualification is essential.

Applications (10 copies), giving the names and addresses of 3 referees, should be received by the undersigned by 28th August, 1958. H. BRIERLEY, House Governor.

METROPOLITAN HOSPITAL, Kingsland-road, London, E.8. (General, 146 Beds.) Applications are invited for the pre-registration post of HOUSE SURGEON, now vacant.

Applications from provisionally and fully registered candidates, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to the Hospital Secretary, as soon as possible.

MILDMAY MISSION HOSPITAL, Austin-street, London, E.2. Applications are invited for the pre-registration post of RESIDENT HOUSE SURGEON (post recognised for F.R.C.S.) vacant now. Candidates should be in sympathy with the evangelical Christian aims of the Hospital.

Applications and references to be addressed to the Medical Superintendent as soon as possible.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited from registered medical practitioners for the appointment of NON-RESIDENT HOUSE PHYSICIAN at The National Hospital, Queen-square, W.C.1, to commence 1st November, 1958. There are 2 vacancies. These posts carry the grade of Senior House Officer. The appointments will be for 6 months.

Applications, with names of 3 referees, to be sent to the undersigned not later than 22nd August, 1958.

H. EWART MITCHELL, Secretary to the Board of Governors.
The National Hospitals for Nervous Diseases,
Queen-square, London, W.C.1.

NORTH MIDDLESEX HOSPITAL, London, N.18. House PHYSICIAN, post-registration, resident, required for 1st October, 1958, for 6 months. General medicine.

Applications (in own handwriting), stating age, nationality, qualifications, experience, with copies of recent testimonials, to Secretary of Hospital, by 28th August, 1958.

NORTH MIDDLESEX HOSPITAL, London, N.18. SENIOR HOUSE OFFICER in Surgery, resident, required, for 1st October, 1958. 6 months' appointment in the first instance, with possible extension to 1 year. General surgery, trauma and orthopædics. Post recognised for F.R.C.S.

Applications, stating age, nationality, qualifications (Primary Fellowship desirable), experience, with copies of recent testimonials and/or names of 2 referees, to Secretary of Hospital by 28th August, 1958.

PRINCESS BEATRICE HOSPITAL, Earl's Court, S.W.5. Applications are invited from fully registered medical practitioners for the post of OBSTETRIC HOUSE SURGEON, with gynæcology and some general surgery. Senior House Officer grade. Resident. Vacancy 9th September, 1958.

Applications to the House Governor as soon as possible, and not later than 26th August, 1958, giving age, qualifications, and 3 testimonials.

PRINCESS BEATRICE HOSPITAL, Earl's Court, S.W.5. Applications are invited for the post of RESIDENT CASUALTY OFFICER (with anæsthetic duties). Senior House Officer grade, recognised for F.R.C.S. Vacancy on 1st September, 1958.

Applications, stating age, qualifications, with 3 testimonials, to the House Governor as soon as possible, and not later than 26th August, 1958.

ROYAL EYE HOSPITAL, St. George's-circus, S.E.1. Applications are invited for the post of SENIOR HOUSE SURGEON from 1st October, 1958. Appointment is for period of 4 months and holder will be eligible for subsequent more senior posts in rotation to a maximum of 20 months. Hospital recognised for the F.R.C.S. and D.O. examinations.

Application forms from Hospital Secretary, to be returned not later than 22nd August, 1958.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited from registered medical practitioners for post of HOUSE SURGEON (resident) for 6 months from 2nd October, 1958. Salary £577 10s. p.a.

Applications to be sent in on a form obtainable from the House Governor by 29th August, 1958.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited for the post of SURGICAL SENIOR REGISTRAR. Appointment will be for 3 or 4 sessions as arranged from October, 1958. Post is open only to candidates who hold Consultant or Senior Hospital Medical Officer sessions elsewhere, or have completed a period of training as Senior Registrars or are from overseas and wish to take a period of advanced training for not more than 2 years. Candidates must hold F.R.C.S. diploma.

Applications on a form obtainable from the House Governor to be submitted by 29th August.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, Brockley Hill, STANMORE, MIDDLESEX. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER for a period of 6 months. Duties to commence 5th October, 1958.

Applications to be received by 3rd September, 1958. Forms of application can be obtained from the House Governor, at 234, Great Portland-street, London, W.1.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer grade), with duties in the E.N.T. Department. Vacant immediately, recognised for F.R.C.S.

Applications, with copies of recent testimonials, to be sent to the Hospital Secretary, by 26th August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for a whole-time appointment as RESIDENT ANÆSTHETIST (second-year Registrar) to fill a vacancy in the approved establishment of the Bermondsey and Southwark Group of hospitals, for duty at St. Olave's Hospital. The salary will be £1071 10s. p.a., and the appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales) and will be for 1 year in the first instance, renewable for a further year.

Applications, giving particulars of age, qualifications, and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 30th August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Anæsthetics to fill a vacancy in the approved trainee establishment at the Camberwell Group of hospitals. The post is recognised for the D.A. and F.F.A. R.C.S. examinations. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, 11, Portland-place, W.1, not later than 30th August, 1958.

SOUTH EAST REGIONAL THORACIC SURGERY UNIT. (50 Beds.) BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER. Recognised for F.R.C.S. 6-month appointment, and may then be renewed for a further period. The work includes surgery for cardiac, œsophageal and tuberculous and non-tuberculous conditions.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. CHARLES' HOSPITAL, Ladbroke-grove, W.10. Locum Tenens SURGICAL REGISTRAR required for 1 month from 1st September.

Applications, stating age, qualifications, experience, together with names and addresses of 2 referees, to Hospital Secretary immediately.

ST. GEORGE'S HOSPITAL, S.W.1, and THE ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL. Applications are invited for the post of SENIOR REGISTRAR to the E.N.T. Department. This is a joint appointment between St. George's Hospital and the Royal National Throat, Nose and Ear Hospital. Candidates should possess the diploma of F.R.C.S. (England).

Applications, stating age, education, qualifications and experience, together with the names and addresses of 2 referees, should reach the undersigned not later than 30th August. The successful candidate will be required to take up duty on, or as soon as possible after, 1st October, 1958.

P. H. CONSTABLE, House Governor, St. George's Hospital.

ST. GILES' HOSPITAL, Camberwell, S.E.5. Senior HOUSE OFFICER (anæsthetics) required from 1st October, 1958. Recognised post for F.F.A. R.C.S. and D.A.

Applications, giving age, qualifications, and details of previous posts, with names of 2 referees or copy testimonials, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, East Dulwich-grove, S.E.22, not later than 1st September, 1958.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE SURGEON for 6 months.

Apply immediately, with 2 recent testimonials, to Hospital Secretary.

ST. MARY'S HOSPITAL (Children's Department), PRINCESS LOUISE KENSINGTON HOSPITAL FOR CHILDREN, St. Quintin-avenue, W.10. E.N.T. AND CASUALTY HOUSE OFFICER post, vacant 1st September, 1958. Recognised for the D.C.H. Post-registration.

Applications, giving full details, with 2 references, to the Secretary, not later than 23rd August, 1958.

ST. MARY'S HOSPITAL, W.2. Anæsthetic Registrar (whole-time) for first period of 12 months from 1st October, 1958. Candidates should possess the D.A.

Applications, with names and addresses of 3 referees, must reach the House Governor not later than 1st September, 1958.

ST. MARY'S HOSPITAL, W.2. Part-time Registrar to the Psychiatric Department (5 sessions per week) for first period of 12 months from 1st October, 1958. Previous experience in psychiatry necessary and preference given to candidates holding the D.P.M.

Full details, with names and addresses of 3 referees, must reach the House Governor by 26th August, 1958.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (Casualty, Orthopædic, and Fracture Departments). Recognised for F.R.C.S. 6-month resident appointment and may then be renewed. Salary £819 10s. p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. NICHOLAS HOSPITAL, Tewson-road, Plumstead, S.E.18. SENIOR HOUSE OFFICER (anæsthetics). The post provides good experience and is recognised for F.F.A. R.C.S. and D.A. 6 months' resident appointment and may then be renewed.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (Casualty Department). Vacant early September. Recognised for F.R.C.S. There are 2 Senior House Officers in the department, which provides good general experience. 6 months' resident appointment, and may then be renewed.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. THOMAS'S HOSPITAL and THE SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. (Joint appointment.) Whole-time SENIOR SURGICAL REGISTRAR at St. Thomas's Hospital and the 3 major Portsmouth hospitals to work mainly at St. Thomas's Hospital, and, subject to annual reappointment, may be required to spend 1 year at Portsmouth.

Applications (9 copies), with names of 2 referees, to the Clerk of the Governors, St. Thomas's Hospital, S.E.1, by 23rd August, 1958.

ST. THOMAS'S HOSPITAL, London, S.E.1. Senior REGISTRAR to the Department of Anæsthetics for a period of 1 year in the first instance. Whole-time.

Applications (5 copies), naming 2 referees, to the Clerk of the Governors by 5th September, 1958.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy in October, 1958, for a JUNIOR ANÆSTHETIC REGISTRAR (Senior House Officer grade).

Further particulars and form of application, which must be returned by 8th September, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy in October, 1958, for a DENTAL HOUSE SURGEON (Senior House Officer grade). The post is recognised for the Fellowship in Dental Surgery, Royal College of Surgeons. Experience is given in oral surgery and orthodontics.

Further particulars and form of application, which must be returned by 8th September, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy in October, 1958, for a Whole-time ASSISTANT MEDICAL REGISTRAR (Registrar grade) with some duties in the Department of Physical Medicine and the Tuberculosis Diagnostic Clinic.

Further particulars and form of application, which must be returned by 8th September, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be vacancies on 15th November, 1958, for the following Senior House Officers :—

1 HOUSE PHYSICIAN.

1 HOUSE SURGEON to the Orthopædic and Plastic Departments.

Further particulars and form of application, which must be returned by 8th September, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 1st November, 1958, for a Whole-time SENIOR REGISTRAR to the E.N.T. Department.

Further particulars and form of application, which must be returned by 8th September, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 1st November, 1958, for a Whole-time REGISTRAR to the Department of Physical Medicine.

Further particulars and form of application, which must be returned by 8th September, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy in October, 1958, for a Whole-time SURGICAL REGISTRAR (Senior Registrar grade).

Further particulars and form of application, which must be returned by 8th September, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE PRIORY, Roehampton, London, S.W.15. 2 Part-time PSYCHIATRIC REGISTRARS required at the above Private Hospital, 1 to be resident. Interesting psychiatric work; suitable for those working for Membership or D.P.M.

Apply Medical Director.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited for post of RESIDENT CASUALTY OFFICER (Senior House Officer grade) with duties as House Physician in Skin Department for 1 year from 1st October, 1958. Board and lodging £150 p.a.

Applications (11 copies), with names of 2 referees, to House Governor by 30th August, 1958.

WHITTINGTON HOSPITAL, London, N.19. Registrar in Clinical Pathology required at Group Laboratory. Some night and weekend duty. Free accommodation when on duty. Post vacant 10th September, 1958. Laboratory may be visited by appointment with the Group Pathologist.

Application forms obtainable from and returnable to Group Secretary, Archway Group Hospital Management Committee, 46, Cholmeley Park, N.6, by 22nd August, 1958.

WOOLWICH GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (pathology). Vacant 1st October. The appointment is to the Group laboratories and is for 1 year. Salary £819 10s. p.a., less £150 p.a. if resident.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (graded Senior House Officer), vacant 12th September, 1958. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c. Recognised for the F.F.A. R.C.S. and D.A.

Applications, stating age, qualifications, and experience, together with copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

ABERYSTWYTH, CARDIGANSHIRE. GENERAL HOSPITAL. MID-WALES HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical) required (resident). Post recognised for F.R.C.S. examination. Vacancy immediate.

Applications, stating age, experience, &c., to the Group Secretary, Mid-Wales Hospital Management Committee, 31, North-parade, Aberystwyth, Cardiganshire.

ALTON GENERAL HOSPITAL. (136 Beds, acute general.) SENIOR HOUSE OFFICER (medical), with anæsthetics. Senior House Officer grade. Post vacant 1st September, 1958.

Applications to Hospital Secretary.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (obstetrics/gynæcology) required at Ashton-under-Lyne General Hospital. Bed complement 75 obstetric and 26 gynæcology. Recognised for M.R.C.O.G.

Applications, with copies of 2 testimonials, to Group Secretary, General Hospital, Ashton-under-Lyne, Lancs.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE.

SENIOR HOUSE OFFICER (general surgery) required at Ashton-under-Lyne General Hospital. Recognised under F.R.C.S. regulations. Vacant September.

HOUSE OFFICER (general surgery) also required.

Applications, with copies of 2 testimonials, to Group Secretary, Ashton-under-Lyne General Hospital, Ashton-under-Lyne, Lancs.

AYLESBURY. ROYAL BUCKINGHAMSHIRE AND ASSOCIATED HOSPITALS MANAGEMENT COMMITTEE. HOUSE SURGEONS (Male or Female). 2 required for the Aylesbury Group Department of Surgery at Tindal General Hospital. Pre-registration posts, but registered practitioners invited to apply. The posts offer wide experience of general surgery with operative practice; recognised for F.R.C.S. The Acute Surgical Unit consists of 85 Beds. No casualty department.

Apply, with copies of 2 testimonials, to the Administrative Officer.

AYRSHIRE. KILMARNOCK INFIRMARY. Senior House OFFICER (orthopædics), now vacant. Married accommodation available. Offers wide experience under specialist supervision. National terms.

Apply immediately, Area Medical Superintendent, 1, Hill-street, Kilmarnock.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON (pre-registration); vacant now. The Hospital serves a wide area of pleasant countryside, and the post affords good opportunity to study excellent clinical material.

Apply to Group Secretary, 19, Alexandra-road, Barnstaple, N. Devon.

BARNSTAPLE. NORTH DEVON INFIRMARY. (Central Group Hospital of 105 Beds.) SENIOR HOUSE SURGEON post vacant immediately for 1 year. Salary £819 10s. p.a. 5-roomed furnished flat available for rental.

Applications, with customary details, to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE PHYSICIAN (pre-registration) required from 5th September, 1958.

Applications, naming 2 referees, to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

BEDFORD GENERAL HOSPITAL. (431 Beds.) House SURGEON required. Pre- or post-registration; recognised for F.R.C.S. Vacant mid-August. Post offers exceptional opportunities for general experience in busy acute surgical units.

Inquiries and applications, with copies of 2 recent testimonials, to be sent immediately to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 acute beds.) ORTHOPÆDIC HOUSE SURGEON with some general surgery (House Officer or Senior House Officer grading according to experience). Vacant now. Approved pre-registration post. Fully registered practitioners may apply. Recognised for F.R.C.S. Married quarters may be available.

Apply Group Secretary.

BIRMINGHAM AND MIDLAND EYE HOSPITAL, Church-street, BIRMINGHAM, 3. CLINICAL ASSISTANT (registered medical practitioner) required in the Glaucoma Clinic for 1 session per week (Friday afternoon). Must possess Diploma in Ophthalmology.

Detailed applications, with names of 2 referees, to the Group Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM, 29. SELLY OAK HOSPITAL. (Equipped beds—1033.) HOUSE SURGEON (pre-registration), now vacant. Recognised for F.R.C.S.

Apply immediately to the Medical Superintendent, giving qualifications, age, experience and enclosing copies of 3 testimonials.

BIRMINGHAM. SELLY OAK HOSPITAL MANAGEMENT COMMITTEE. Locum REGISTRAR in Radiology required for 4 months (October, 1958–January, 1959), for Selly Oak Hospital (1033 Beds) with associated Maternity, Eye, E.N.T., and Infectious Diseases Hospitals. All forms of radiodiagnostic work undertaken.

Applications in writing to Secretary, Oak Tree-lane, Birmingham, 29.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Stoke-on-Trent Group, Princes-road, Stoke-on-Trent

(*a*) REGISTRAR (E.N.T. surgery). Main duties North Staffordshire Royal Infirmary. Recognised F.R.C.S. and D.L.O. Post offers excellent experience. Medical library facilities.

(*b*) REGISTRAR (orthopædics), North Staffordshire Royal Infirmary (455 Beds.) Resident or non-resident. Some duties at Hartshill Orthopædic Hospital (77 Beds). Experience specialty essential. Higher qualifications an advantage.

Application forms from Group Secretary, to be returned by 25th August, 1958.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. RESIDENT MEDICAL OFFICER (Senior House Officer). General Hospital with 5 other resident medical officers.

Apply Medical Superintendent.

BIRMINGHAM. ST. CHAD'S HOSPITAL, Hagley-road, BIRMINGHAM, 16. HOUSE SURGEON required. Recognised for pre-registration.

Detailed applications, with copies of testimonials, to Group Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM. ST. MARGARET'S HOSPITAL, Great BARR, BIRMINGHAM, 22a. (Mental Deficiency—1491 Beds.) RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER. Accommodation for single person only.

Applications, stating age, qualifications and experience, together with names and addresses of 3 referees, should be forwarded to the Medical Superintendent not later than 30th August, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of REGISTRAR in Pathology. The post is tenable for 1 year in the first instance, from 1st October, 1958. The successful candidate will take part in a training scheme to be instituted in collaboration with the division of pathological studies, University of Birmingham, providing for experience in all branches of pathology and work in various specialised hospitals within the United Hospitals.

Further information concerning the appointment, and forms of application, may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned by 30th August, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of CASUALTY SURGICAL REGISTRAR (with orthopædic experience) (Registrar grade) to the United Birmingham Hospitals, for duty in the Casualty Department at the General Hospital. Candidates should hold at least a Primary Fellowship qualification. The successful candidate will be required to be resident on rota. A scheme for the interchange, at the level of Registrar, between the Casualty Department of the General Hospital and one of the Registrar appointments at the Royal Orthopædic Hospital has been agreed between the United Birmingham Hospitals and the Birmingham Regional Hospital Board, and the successful candidate may be required to spend not more than a year in such interchange.

Forms of application from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, to be returned by 30th August, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. QUEEN ELIZABETH HOSPITAL. Applications are invited for the resident appointment of HOUSE SURGEON to the Ophthalmic Department for the period ending 6th January, 1959. Recognised for pre-registration candidates, but registered medical practitioners may apply.

Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned as soon as possible.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of SURGICAL REGISTRAR (Registrar grade) to the Surgical Professorial Unit, United Birmingham Hospitals. Candidates must have held a resident appointment and should have the F.R.C.S. The successful candidate will be required to take part in a rota of resident duties.

Forms of application from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, to be returned by 30th August, 1958.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. Locum ANÆSTHETIC REGISTRAR (resident) required full-time for period 8th–21st September, 1958, inclusive.

Applications to Hospital Secretary. Telephone: Bishop's Stortford 963.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. Applications invited for post of HOUSE OFFICER (surgical—pre-registration). Salary £467 10s.–£522 10s. p.a. less £125 for residential emoluments. Appointment to commence immediately.

Applications, stating age, nationality, qualifications and experience, with copies of 2 testimonials or names of referees, to Hospital Secretary.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. Applications are invited for the post of HOUSE OFFICER (medical—pre-registration). Salary £467 10s.–£522 10s. p.a., less £125 in respect of residential emoluments. Appointment to commence 10th September, 1958.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, or names of referees, to Hospital Secretary.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics) required immediately for duties throughout the Group, mainly at Royal Infirmary, Blackburn. Residence at Royal Infirmary, Blackburn. Post recognised for D.A. and F.F.A. R.C.S.

Applications to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn, giving names of 2 referees.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Royal Infirmary, Blackburn

HOUSE SURGEON required immediately. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Queen's Park Hospital, Blackburn

HOUSE SURGEON required immediately. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Victoria Hospital, Accrington

HOUSE PHYSICIAN required immediately. Post recognised for pre-registration purposes.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN. ROYAL INFIRMARY. (262 general beds.) BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (casualty and orthopædics) required 11th September, 1958. Recognised for F.R.C.S.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKPOOL VICTORIA HOSPITAL. Casualty Officer (Junior Hospital Medical Officer grade). This post, now vacant, is recognised for the F.R.C.S. and offers a variety of experience in a busy department. Residence is optional.

Applications, stating age, qualifications, experience, and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE OFFICER (orthopædic and traumatic surgery). Resident pre-registration post recognised for F.R.C.S., available in the main acute General Hospital serving the Blackpool and Fylde area.

Applications, stating age, experience (if any), and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the post of HOUSE PHYSICIAN to the Geriatric Unit. This is a large Unit with an active rehabilitation section, which provides excellent clinical facilities. Vacant 16th September, 1958.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, 7.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON (orthopædics). Salary in accordance with national scale. This is a pre-registration appointment.

Applications, stating age, qualifications, and experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

BRIGHTON. NEW SUSSEX HOSPITAL FOR WOMEN AND SUSSEX MATERNITY HOSPITAL. BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. GYNÆCOLOGICAL AND OBSTETRIC HOUSE SURGEON (Female) required 17th September, 1958. Gynæcological Department (24 Beds) at New Sussex Hospital and relief obstetrical work at Sussex Maternity Hospital (62 Beds). Post recognised for M.R.C.O.G.

Applications, giving age, experience, and 2 references, to be sent to the Administrative Officer, New Sussex Hospital, Windlesham-road, Brighton, by 21st August, 1958.

BRIGHTON. ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, Dyke-road, BRIGHTON. BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. (137 Beds and Cots.) Vacancy for HOUSE PHYSICIAN for 6 months. The post offers wide experience in paediatrics and is recognised for D.C.H.

Applications, stating age, nationality, qualifications, and experience, together with copies of recent testimonials, to be sent to the Administrative Officer as soon as possible.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) CASUALTY HOUSE SURGEON required end August. Duties include work in orthopædic and traumatic unit. Recognised for pre-registration and F.R.C.S.

Applications, stating age, qualifications, experience, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) RESIDENT ANÆSTHETIST (Senior House Officer grade) required for 1 year, with interchange of duties, by agreement, at the Brighton General Hospital and other specialised units within the Brighton and Lewes Group. Post recognised for F.F.A. R.C.S. and D.A.

Applications, stating age, qualifications, experience, &c., and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. SUSSEX EYE HOSPITAL. (56 Beds.) HOUSE SURGEON required end of August. Recognised for F.R.C.S. and D.O. Successful applicant will be considered for post of Senior House Surgeon on completion of 6 months.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BURNLEY AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER to Orthopædic and Casualty Departments. Recognised for F.R.C.S. Resident accommodation available. Post available September.

Applications, with the names of 2 referees, to Group Secretary, Burnley General Hospital.

BURNLEY AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. BURNLEY GENERAL HOSPITAL (641 Beds), BURNLEY VICTORIA HOSPITAL (171 Beds). RESIDENT HOUSE OFFICERS (surgical). The appointments are approved as pre-registration posts and recognised for F.R.C.S. Subject to satisfactory service, the successful applicants will be favourably considered for appointment as House Physician at the termination of contract as Surgical House Officer.

Applications, with 2 references, to Group Secretary, Burnley General Hospital.

BURNLEY VICTORIA HOSPITAL. (171 Beds.) Burnley AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE OFFICER (medical). The appointment is approved as a pre-registration post. Post now available.

Applications, with 2 references, to Group Secretary, Burnley General Hospital.

BRISTOL. FRENCHAY HOSPITAL. Applications invited for appointment of SENIOR HOUSE OFFICER in the regional department of thoracic surgery (100 Beds). Post provides experience in cardiac, œsophageal and pulmonary surgery, and is recognised for Fellowship Examinations of the Royal College of Surgeons. Vacant 1st September, 1958, tenable for 6 months, renewable by mutual agreement.

Apply to Group Secretary, Frenchay Hospital, Bristol, stating age and experience, and naming 2 referees.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE OFFICER (orthopædics) (pre-registration post) required at the above Hospital. Recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of Pre-registration HOUSE OFFICER in Surgery for duties at the Bury and Rossendale General Hospitals.

Apply, stating full details, to H. WILKINSON, Group Secretary, Bury General Hospital, Walmersley-road, Bury.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) GYNÆCOLOGICAL HOUSE SURGEON required at Highland Court Annexe, a unit of 25 gynæcological beds situated 3 miles from the above Hospital, with all ancillary services available. Recognised for M.R.C.O.G. 6 months' appointment. Post vacant mid-September. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of PÆDIATRIC HOUSE PHYSICIAN, recognised for D.C.H., includes work in the ward and Outpatient Department and also provides experience in the care of the newborn. Opportunities exist for the study of preventive medicine among children and child guidance work. Post vacant end of September, 1958. National Health Service salary and conditions.

Applications, together with copies of 2 testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (casualty) which becomes vacant mid-September, 1958. Salary £819 10s. p.a. Recognised for the F.R.C.S.

Applications to be sent to the Hospital Secretary at the above Hospital, together with copies of 3 recent testimonials.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 550 Beds.) RESIDENT MEDICAL REGISTRAR required. Recognised for D.C.H.

Applications, on forms obtainable from the Group Secretary, should be returned by 23rd August, 1958.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. (733 Beds.) Locum ANÆSTHETIC REGISTRAR required 15th September–9th December inclusive.

Apply to Group Secretary.

CHELMSFORD, ESSEX. BROOMFIELD HOSPITAL. Required, experienced Locum Tenens SENIOR REGISTRAR for 6 months from 1st September, 1958, full residence or only when on duty. Unit has 312 Beds for the treatment of pulmonary tuberculosis in adults. Tuberculous and non-tuberculous thoracic surgery, chest clinics, and mass radiography.

Apply Physician-Superintendent.

CHELMSFORD HOSPITAL MANAGEMENT COMMITTEE. Locum SENIOR HOUSE OFFICER ANÆSTHETIST required for period 21st–28th September. Resident.

Applications to Secretary, London-road, Chelmsford, Essex.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL. (430 Beds.) ANÆSTHETIC REGISTRAR required. Post recognised for F.F.A. R.C.S. and D.A. Hospital may be visited by arrangement with Physician-Superintendent (telephone: Ottershaw 441).

Application forms from Secretary, Woking and Chertsey Hospital Management Committee, Huntington, Guildford-road, Chertsey, Surrey. Closing date 1st September.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL. WOKING AND CHERTSEY GROUP. (430 Beds.) ROYAL SURREY COUNTY HOSPITAL, GUILDFORD GROUP. (233 Beds.) Locum Full-time E.N.T. REGISTRAR for above and other hospitals in the Groups concerned required from 30th August, 1958, to 14th December, 1958. Recognised for F.R.C.S. and D.L.O. The hospitals may be visited by arrangement.

Applications to Physician-Superintendent, St. Peter's Hospital. Telephone: St. Peter's Hospital, Ottershaw 441; Royal Surrey County Hospital, Guildford 2323.

CHERTSEY, SURREY. BOTLEYS PARK HOSPITAL. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR (psychiatry). This modern Mental Deficiency Hospital of 1550 Beds provides full facilities for patients of all grades. Applications are especially invited from those with pædiatric experience and interest in the problem of physically defective and mentally retarded children. Accommodation available for single person.

Application forms obtainable from the Secretary to the Hospital Management Committee.

CHESTERFIELD. SCARSDALE HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER required 1st September for Geriatric Unit and for duties at Penmore Hospital. Full Consultant services. Excellent scope for doctor interested in this specialty. House available on service tenancy.

Applications, giving full particulars, with the names of 3 referees, to Group Secretary, Chesterfield Hospital Management Committee, at Chesterfield Royal Hospital.

CHESTERFIELD ROYAL HOSPITAL. Casualty Officer (Senior House Officer) required end September. Post recognised F.R.C.S. purposes.

Apply, with copies of testimonials, or names of 2 referees, to the Group Secretary, Chesterfield Hospital Management Committee, immediately, from whom particulars are obtainable.

CHESTER-LE-STREET. GENERAL HOSPITAL. (204 Beds.) SENIOR HOUSE OFFICER (general medicine). Post now vacant.

Apply, with names and addresses of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

CHESTER-LE-STREET. GENERAL HOSPITAL. (204 Beds.) HOUSE PHYSICIAN (general medicine). Approved pre-registration post. Post now vacant.

Apply, with names and addresses of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE: Applications invited for:—

Black Notley Hospital, Braintree, Essex (522 Beds)

Post of Locum REGISTRAR for Pulmonary Tuberculosis Unit, including non-tuberculous diseases of the chest; also duties at chest clinics. Required 1st September for few months.

Essex County Hospital, Colchester, Essex (181 Beds)

Post of Locum SURGICAL REGISTRAR. Required early September.

Post of SENIOR HOUSE OFFICER to Casualty and Radiotherapy Departments. Tenable for 6 months or 1 year. Recognised for F.R.C.S.

Clacton and District Hospital, Clacton-on-Sea, Essex (58 Beds)

Post of TEMPORARY REGISTRAR required as Resident Casualty Officer for 2–3 months.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CREWE AND DISTRICT MEMORIAL HOSPITAL. (108 Beds—acute, and continuation 32 Beds.) SENIOR HOUSE OFFICER (casualty) required. Approved for F.R.C.S. Now vacant. Modern well-equipped department.

Apply immediately, stating age, qualifications, &c., with names of 2 referees, to reach the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire, within 7 days.

CROYDON. MAYDAY HOSPITAL. (595 Beds.) Croydon GROUP HOSPITAL MANAGEMENT COMMITTEE. ORTHOPÆDIC HOUSE OFFICER (Senior House Officer grade) required for 6 months in first instance. Post vacant 18th August, 1958.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon.

CROYDON. MAYDAY HOSPITAL. (595 Beds.) Croydon GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum Tenens SURGICAL REGISTRAR for 10 weeks from 25th August, 1958. Post resident or non-resident.

Applications in writing, with names of 2 referees, to GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon, Surrey, by 19th August.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH. MID-SUSSEX HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (general surgery). Post recognised for Fellowship, vacant 1st September, 1958.

Apply Hospital Secretary, stating age, qualifications, nationality, and experience, with names of 2 referees.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER (casualty). Vacant 22nd September, resident post. Recognised for periods of 6 months' casualty training for F.R.C.S. The staffing of the department is a Senior Casualty Officer and 2 Senior House Officers.

Apply, stating age, experience, and 2 names for reference to Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER (orthopædic). Vacant 1st September. Recognised for 6 months' "unspecified" training for F.R.C.S.

Apply, giving full details and 2 names for reference, to Secretary.

DEWSBURY, YORKSHIRE. THE GENERAL HOSPITAL. (128 Beds.) Applications are invited for the pre-registration post of HOUSE PHYSICIAN (general medicine and pædiatrics) which is now vacant.

Applications, giving full details, should be sent to the Administrative Officer at the Hospital as soon as possible.

DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL HOSPITAL. (247 Beds.) HOUSE SURGEON (first, second or third post). Vacant now. General surgery, casualty and some orthopædics. Approved pre-registration post. Fully registered practitioners may apply. Married quarters may be available.

Applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

DORCHESTER, DORSET. HERRISON HOSPITAL. JUNIOR HOSPITAL MEDICAL OFFICER. This Hospital, which is situated in delightful country, invites application from a progressive young practitioner prepared to accept clinical responsibility. The Hospital is building a new Admission Block of most modern design and is expanding its activities. Facilities for attendance at Outpatient, Child Guidance, and Neurological Clinics are available, and there are opportunities for original work. A small self-contained flat is available. The Hospital may be visited by appointment.

Applications, giving age, qualifications, experience and the names of 2 referees, should be sent to the Medical Superintendent.

DORCHESTER. DORSET COUNTY HOSPITAL. House SURGEON (Male or Female) required for resident, pre-registration post now vacant. Recognised for F.R.C.S. examination and tenable for 6 months.

Applications, stating age, qualifications, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

DORCHESTER. DORSET COUNTY HOSPITAL. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD. WEST DORSET GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum SURGICAL REGISTRAR (Registrar grade) required from 1st September, 1958, for 8 weeks. Salary £19 5s. per week, less £170 p.a. if resident.

Applications, giving details of age, qualifications and experience, together with names of 3 referees, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP, BIRMINGHAM REGION.

The Guest Hospital, Dudley (154 Beds)

SENIOR HOUSE OFFICER (anæsthetics). Post recognised for F.F.A. R.C.S. and D.A. Successful candidate will be required to visit other hospitals in the Group.

Applications, giving the names of 2 referees, to the Group Secretary, Guest Hospital, Dudley, Worcs.

HOUSE OFFICER (surgical), pre-registration. Post vacant now.

HOUSE OFFICER (medical), pre-registration. Post vacant now.

Prestwood Sanatorium, near Stourbridge (199 Beds—tuberculosis)

JUNIOR HOSPITAL MEDICAL OFFICER. Resident required for a period of 1 year in the first instance.

Apply Group Secretary, Guest Hospital, Dudley, Worcs.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. REGISTRAR in Ophthalmology, Norfolk and Norwich Hospital, Norwich (441 Beds). Recognised for D.O. and F.R.C.S.

ORTHOPÆDIC REGISTRAR, Norfolk and Norwich Hospital, Norwich (441 Beds). Post recognised for F.R.C.S.

SURGICAL REGISTRAR, Norfolk and Norwich Hospital, Norwich (441 Beds). Recognised for F.R.C.S.

ANÆSTHETIC REGISTRAR, West Norfolk and King's Lynn Hospital, King's Lynn (146 Beds). Post provides wide experience and recognised for D.A. Single accommodation available now. Married quarters will be available in approximately 6 months.

Candidates invited to visit Hospitals by direct arrangement with Hospital Management Committee Secretary at the Hospitals.

PÆDIATRIC REGISTRAR, Jenny Lind Children's Hospital, Norwich (76 Beds). Recognised for D.C.H. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary, Norfolk and Norwich Hospital, Norwich.

REGISTRAR in Geriatrics, Ipswich and East Suffolk Hospital Group. New area service in course of development under Consultant Physician in Geriatrics. Duties at unit in Ipswich and East Suffolk Hospital and other hospitals in the area. Candidates invited to visit hospitals by direct arrangements with Hospital Management Committee Secretary, Ipswich and East Suffolk Hospital, Anglesea-road Wing, Ipswich.

All appointments for 1 year, renewable for second year.

Applications, stating age, experience, and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 1st September, 1958.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. RESIDENT PÆDIATRIC HOUSE PHYSICIAN for above Hospital. Post vacant 24th September, 1958. 6 months' appointment. Post recognised for pre-registration purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Administrator of Hospital by 22nd August, 1958.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. Locum CASUALTY OFFICER (Registrar grade) required for period 1st–20th September, 1958. Non-resident.—Hours: 9 A.M.–5.30 P.M. Monday to Friday; 9 A.M.–1 P.M. Saturday.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. Locum OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR required for obstetric and gynæcological duties from 1st September, 1958, for period of not less than 6 weeks. M.R.C.O.G. desirable. Non-resident appointment, but will be required to sleep in when on duty.

Applications, with names and addresses of 2 referees, to Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. Appointment of RESIDENT HOUSE SURGEON (third post). Vacant now. Post provides experience and duties in both general surgery and orthopædics. 6 months' appointment. Post recognised for F.R.C.S. by the Royal College of Surgeons.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, at Chase Farm Hospital.

FARNBOROUGH HOSPITAL, Kent. (100 Beds.) House SURGEON required 5th September. Recognised for F.R.C.S. Pre-registration post.

Apply, stating age, qualifications (with dates), and experience, and naming 3 referees, to Administrative Officer by 26th August, 1958. (Ref. H.S.)

GLASGOW, N.W. RUCHILL HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in the Infectious Diseases Department (450 Beds). Excellent experience in infectious diseases and general medicine. Undergraduate and postgraduate teaching unit and regional centre for treatment of poliomyelitis.

Applications, stating age, nationality, qualifications and experience, with names of 2 referees to Physician-Superintendent.

GRANTHAM AND KESTEVEN GENERAL HOSPITAL. (117 Beds.) (Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL REGISTRAR required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th August, 1958, giving age, nationality, qualifications, present and previous appointments (with dates), naming 3 referees.

GRIMSBY GENERAL HOSPITAL. Grimsby Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædics). Orthopædic Unit of 58 Beds. Resident establishment Registrar and 2 House Officers. Up-to-date medical library and reading facilities available.

Applications, with names of 2 referees, to Hospital Secretary.

GRIMSBY. SCARTHO ROAD HOSPITAL. (255 Beds.) (Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL REGISTRAR required. Furnished married accommodation available if required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th August, 1958, giving age, nationality, qualifications, present and previous appointments (with dates), naming 3 referees.

GUILDFORD. ST. LUKE'S HOSPITAL. Guildford GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL BOARD. Applications are invited for the post of REGISTRAR (obstetrics and gynæcology), 1 of 2. Post offers extensive experience in obstetrics and gynæcology. Possession of higher qualification an advantage. The post is recognised for the M.R.C.O.G. Hospital may be visited by arrangement direct (telephone: Guildford 62851, extension 37).

Application forms from Secretary, Guildford Group Hospital Management Committee, St. Luke's Hospital, Guildford, to whom they should be returned by 23rd August, 1958.

HAILSHAM, SUSSEX. HELLINGLY HOSPITAL. Hailsham HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners (Male or Female) for the whole-time post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital. The post is a trainee appointment and offers experience in all branches of adult psychiatry. In addition, opportunities can be afforded for some experience in neurology and mental deficiency. The Hospital has a high admission-rate and is recognised for the D.P.M. Married or single accommodation is available.

Applications, giving the names of 3 referees, should be sent to the Medical Superintendent within 14 days of the appearance of this advertisement.

HASTINGS AND ST. LEONARDS. BUCHANAN HOSPITAL. (91 Beds.) Locum SENIOR HOUSE OFFICER (obstetrics) required, 8th–15th September, 1958, inclusive. Salary £15 19s. a week, less board.

Apply, with names of 2 referees, to the Administrator, Buchanan Hospital, St. Leonards-on-Sea.

HASTINGS GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum RESIDENT SURGICAL OFFICER (general surgery) required 23rd August–20th September, 1958. Salary £19 5s. per week. Non-resident.

Applications, with copies of 2 testimonials or names of 2 referees to Group Secretary.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) HOUSE SURGEON. Pre-registration post for general surgery and urology required at this acute hospital (surgical). Post vacant 1st October, 1958.

Applications, with names of 2 referees, to Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Applications are invited for the post of CASUALTY AND ORTHOPÆDIC HOUSE SURGEON (1 of 2 posts), graded Senior House Officer, for the Royal East Sussex Hospital, Hastings. Modern department. Hospital is pleasantly situated facing the sea. Post vacant 22nd August, 1958.

Applications, with names of 2 referees, to the Administrator.

HASTINGS. ST. HELEN'S HOSPITAL. (491 Beds.) SENIOR HOUSE OFFICER (geriatrics) required. Resident post. Staff of 5. Post vacant now.

Applications immediately to Hospital Administrator.

HITCHIN, HERTFORDSHIRE. NORTH HERTS HOSPITAL. HOUSE SURGEON required. Post vacant end of August. Recognised as pre-registration post.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to the Medical Administrator, Lister Hospital, Hitchin, as soon as possible.

HORNCHURCH. ST. GEORGE'S HOSPITAL. Junior HOSPITAL MEDICAL OFFICER (resident) required from approximately 1st September next at this Hospital which accommodates 404 chronic sick patients. The post offers excellent geriatric experience.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford, as soon as possible.

HOVE GENERAL HOSPITAL. Pre-registration House PHYSICIAN required for a period of 6 months from 4th September, 1958. Excellent clinical material available and post is suitable for candidate working for a higher degree.

Applications, stating age, qualifications and full details of experience, together with names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Sackville-road, Hove, 3.

HOVE GENERAL HOSPITAL. House Surgeon (pre-registration) with ward and casualty duties required for a period of 6 months from 1st September, 1958. This post is recognised for the F.R.C.S. and provides a wide experience in an active surgical unit.

Applications, stating age, qualifications, and full details of experience, together with names and addresses of 2 referees, to the Administrative Officer, Hove General Hospital, Sackville-road, Hove, 3.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.
The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN to commence duties immediately. The post is recognised as a pre-registration appointment. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Group Secretary,
Huddersfield Hospital Management Committee.
The Royal Infirmary, Huddersfield.

HEMEL HEMPSTEAD, HERTFORDSHIRE. ST. PAUL'S HOSPITAL. HOUSE PHYSICIAN (pre-registration) required to commence 4th October, 1958.

Applications, giving details and enclosing copies of 2 recent testimonials, should be sent to the Hospital Secretary.

HEREFORD GENERAL HOSPITAL. (154 Beds.) House OFFICER (general surgery) required immediately. Pre-registration post. Hospital recognised by R.C.S. Duties include care of general surgical beds, and in addition for 3 months of orthopædic beds and for 3 months of E.N.T. beds.

Applications, with copies of 2 testimonials, to be sent to the Group Secretary, Victoria House, Eign-street, Hereford.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE SURGEON (recognised for the F.R.C.S. examinations). Pre-registration post.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE PHYSICIAN. Pre-registration post.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE PHYSICIAN. Duties in an active Geriatric Unit for the investigation and treatment of acute and long-term illness. Post vacant 1st September, 1958.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. HOUSE SURGEON or Locum HOUSE SURGEON required immediately. An interesting and varied post and recognised for D.C.H.

Applications, together with details of experience, giving the names of 2 referees, should be sent to the Hospital Secretary.

HUNTINGDON COUNTY HOSPITAL. Applications are invited for the post of HOUSE OFFICER (medical), now vacant. The selected candidate will be required to look after medical and pædiatric cases and may be called upon to give emergency anæsthetics.

Apply, with full particulars and names of 2 referees, to Secretary, County Hospital, Huntingdon.

HUNTINGDON COUNTY HOSPITAL. Locum Tenens HOUSE PHYSICIAN required now. Work includes care of medical and pædiatric cases, and the administration of emergency anæsthetics.

Apply, with full particulars and names of 2 referees, to Secretary, County Hospital, Huntingdon.

HUNTINGDON COUNTY HOSPITAL. Locum Tenens HOUSE SURGEON required now for an appointment of approximately 6 weeks' duration.

Apply, with full particulars and names of 2 referees, to Secretary, County Hospital, Huntingdon.

KETTERING AND DISTRICT GENERAL HOSPITAL. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. The post, vacant early September, 1958, offers wide experience of all traumatic conditions including fractures and some orthopædic cases, with charge of 30 Beds.

Applications, accompanied by testimonials, to be sent to the Group Secretary, General Hospital, Kettering.

KETTERING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER to the Geriatric Unit in this area. There are 160 active beds in the unit in 3 hospitals. Post now vacant. Married residential accommodation available. National scale of salary.

Applications, together with the names and addresses of 2 referees, to the Group Secretary, Central Administration Offices, General Hospital, Kettering.

KIDDERMINSTER AND DISTRICT GENERAL HOSPITAL. (112 Beds.) Applications are invited for the appointment of Part-time CLINICAL ASSISTANT in General Surgery, which will be for 6 sessions per week at the rate of £183 15s. per session p.a.

Full particulars of the appointment may be obtained from the Secretary of the Mid-Worcestershire Hospital Management Committee, Birmingham-road, Bromsgrove, to whom applications should be addressed.

KINGSTON UPON THAMES. KINGSTON HOSPITAL, Wolverton-avenue, KINGSTON UPON THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (E.N.T.), which is available on 1st October, 1958. The post is recognised for D.L.O. purposes.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital within 7 days of the appearance of this advertisement.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (350 Beds.) Applications invited for post of HOUSE SURGEON to the Senior Consultant General Surgeon, vacant mid-September. Post recognised for pre-registration and F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (350 Beds.) Applications invited for post of HOUSE SURGEON to Fracture and Orthopædic Department, vacant mid-September. Approved pre-registration post.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH. ST. HELEN'S HOSPITAL. (129 Beds for infectious diseases, pulmonary tuberculosis, long-stay orthopædics and geriatrics. The area Chest Clinic is in the Hospital.) HOUSE PHYSICIAN required (post-registration appointment). Accommodation available for married man.

Applications to JOHN WILLIAMS, Group Secretary, Ipswich Group Hospital Management Committee, at the Ipswich and East Suffolk Hospital (Anglesea-road Wing), Ipswich.

ILKLEY. MIDDLETON HOSPITAL. (386 Beds.) RESIDENT SENIOR HOUSE OFFICER (surgical) required for Major Thoracic Surgical Unit at the above Hospital. Eminently suitable for person intending to take Membership or Fellowship examination.

Applications, stating age, nationality, qualifications and experience, to Hospital Secretary.

LANCASTER. BEAUMONT HOSPITAL. Resident SENIOR HOUSE OFFICER (E.N.T.) for a newly constructed self-contained ward and theatre unit, with attendance at outpatients at Lancaster, Kendal, and Morecambe.

Applications, with names of 2 referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster.

LANCASTER. ROYAL LANCASTER INFIRMARY. (240 Beds.) SENIOR HOUSE OFFICER (medical). Duties include care of acute cases under the supervision of 2 Consultant Physicians and attendance at Consultative Clinics. The post is normally tenable for 1 year. The post is vacant 1st September next.

Applications, with names of 2 referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster.

LANCASTER. ROYAL LANCASTER INFIRMARY. (240 Beds.) SENIOR HOUSE OFFICER (casualty). The successful applicant will work with the specialist orthopædic unit. The post, recognised for F.R.C.S., is vacant 18th August 1958.

Applications, with names of 2 referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster.

LEAMINGTON SPA. WARNEFORD GENERAL HOS-PITAL. (197 Beds.) Locum HOUSE PHYSICIAN required, 12th–25th September inclusive.

Apply Hospital Secretary.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Chest Diseases

(i) Leeds Chest Clinic and additional duties, as required, at Regional Sanatoria. Previous experience in diseases of the chest desirable. Accommodation for a single person only at Killingbeck Hospital.

(ii) Scotton Banks Sanatorium, Knaresborough (150 staffed beds). Visiting staff includes Teaching Hospital Consultants. Preferably resident.

Obstetrics and Gynæcology

Leeds A Group. Duties to alternate (6-month periods) between St. Mary's Hospital, Leeds (109 obstetric beds), and St. James's Hospital, Leeds (75 obstetric and 52 gynæcological beds). Resident. Recognised for M.R.C.O.G.

Infectious Diseases

Leeds Road Hospital, Bradford (120 infectious diseases beds). Accommodation for a single person only.

Ophthalmology

Hospital Eye Department, Halifax. 18 Beds with special theatre and outpatient unit.

Otolaryngology

Huddersfield and Halifax Groups (non-resident). Successful candidate to reside in Huddersfield. Recognised for the Fellowship and the D.L.O.

Psychiatry

Stanley Royd Hospital, Wakefield (2000 Beds). Recognised for D.P.M. If desired facilities for attendance at the University of Leeds will be provided if the successful candidate is studying for the D.P.M.

Applications, stating age, qualifications, and details of present and previous appointments (with dates), together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 27th August, 1958.

LEEDS. THE UNITED LEEDS HOSPITALS. Applications are invited for the post of HOUSE SURGEON (pre-registration) or SENIOR HOUSE OFFICER at the Chapel Allerton Hospital Leeds. Post vacant now. The post offers experience in surgical neurology, E.N.T., and ophthalmic surgery. The officer will work under the Consultants of the General Infirmary, and the post offers facilities for study for higher qualifications.

Applications, stating age, qualifications, and the names of 3 referees, should be sent immediately to the Secretary to the Board, The General Infirmary, Leeds, 1.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. HOUSE OFFICERS required in the Departments of Urology and Neurosurgery. The posts are tenable for 6 months from 1st August, 1958. Salary according to grade. Terms and conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts (with dates), and 3 names for reference, to be sent to the Secretary to the Board, The General Infirmary, Leeds, 1, immediately.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. RESIDENT SURGICAL OFFICER of Registrar status required for 1 year in the first instance. Terms and conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts (with dates), and 3 names for reference, should be sent to the Sub-Dean, School of Medicine, Leeds, 1, not later than 30th August, 1958.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. Applications are invited for the post of REGISTRAR in the Department of Psychiatry (Leeds University) to work at the General Infirmary at Leeds. Some previous experience in psychiatry necessary. Facilities are available for attendance at the course of the Leeds University D.P.M. or for preparation for a higher degree.

Applications, including the names of 3 referees, should be sent to the Sub-Dean, School of Medicine, Leeds, 2, by not later than 30th August, 1958.

LINCOLN COUNTY HOSPITAL. (200 Beds.) Applications are invited from Men and Women for the resident post of SENIOR HOUSE OFFICER in Medicine which is vacant immediately and tenable for 6 months.

Applications, with copy testimonials, should be sent to the Secretary.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. The following House Officer posts are still available for pre-registration or registered applicants for the 6 months beginning 1st September, 1958 :—

ORTHOPÆDIC HOUSE SURGEONS at David Lewis Northern Hospital and Royal Liverpool Children's Hospital.

HOUSE SURGEONS at Liverpool Stanley Hospital and Royal Liverpool Children's Hospital Heswall Branch.

HOUSE PHYSICIAN at Royal Liverpool Children's Hospital Heswall Branch.

HOUSE SURGEON (gynæcology) at Liverpool Stanley Hospital.

Apply immediately on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LOUTH, LINCOLNSHIRE. COUNTY HOSPITAL. (215 Beds.) GRIMSBY HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical). Applications are invited for this pre-registration post, vacant middle of August, 1958.

Applications, giving full details, together with the names of 2 referees, should be addressed to the Hospital Secretary.

MANCHESTER, 20. WITHINGTON HOSPITAL. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade). Previous experience in pathology not essential, the post affording opportunities for gaining experience in all branches of clinical pathology.

Applications, stating age, qualifications, present post, experience, and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER, 20. WITHINGTON HOSPITAL. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (orthopædics) required at the above Hospital, vacant from October, 1958. This post offers excellent experience for persons who ultimately intend to specialise in orthopædics and accident work. In addition to the routine orthopædic duties of a general hospital the unit carries out the reconstructive surgical programme of patients from the Devonshire Royal Hospital, Buxton, which has a regional catchment area.

Applications, with full details and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, as soon as possible.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of CASUALTY OFFICER (Junior Hospital Medical Officer grade) at the above Hospital.

Applications, stating age, qualifications, present post, and names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement.

MANCHESTER. UNITED MANCHESTER HOSPITALS, MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. SENIOR HOUSE OFFICER to Department of Hæmatology, to commence as soon as possible. Whole-time, non-resident post, tenable for 6 months, renewable for a second and possibly a third 6 months.

Application form obtainable from the Secretary, to be returned immediately.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER.

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.

Manchester Royal Eye Hospital.

MANCHESTER. UNITED MANCHESTER HOSPITALS. ROYAL EYE HOSPITAL, MANCHESTER, 13. SENIOR REGISTRAR in Ophthalmology. Whole-time, non-resident post, tenable for 12 months, renewable. Previous experience essential.

Application form obtainable from the Secretary to the Board of Governors, United Manchester Hsopitals, Manchester Royal Infirmary, Manchester, 13, to be returned as soon as possible.

MANCHESTER REGIONAL HOSPITAL BOARD. Bury AND ROSSENDALE and ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEES. Applications are invited for the post of REGISTRAR in Paediatrics which will be vacant on 30th September, 1958. The successful applicant, who may be either resident or non-resident, will have duties in the neonatal departments and children's units at hospitals in the above Groups, which are recognised for the D.C.H. The person appointed to the post will supervise the work of Senior House Officers in both Groups and assist the Consultant Paediatrician.

Apply, stating full details of experience and qualifications, together with names of 2 referees, to H. WILKINSON, Group Secretary, Bury General Hospital, Bury, Lancs.

MANCHESTER REGIONAL HOSPITAL BOARD. Resi-DENT SURGICAL REGISTRAR required 1st November, 1958, for the Royal Infirmary, Blackburn, a busy acute hospital of 262 Beds. Post recognised for F.R.C.S.

Application forms available from Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of REGISTRAR in Thoracic Surgery to the Blackpool and Fylde Group of hospitals with main duties at the Victoria Hospital, Blackpool. The post, available from 5th September, is recognised for the F.R.C.S. and offers a sound experience gained with 2 Consultant Thoracic Surgeons who are responsible for the thoracic surgery in the Northern part of the Manchester Region. Non-resident post, but residential accommodation is available if required for single applicants.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, should be sent to the Group Secretary, Victoria Hospital, Blackpool.

MANCHESTER REGIONAL HOSPITAL BOARD invites applications for the post of RESIDENT REGISTRAR in General Surgery, vacant 29th September, 1958. The duties will be with the Stockport and Buxton Hospital Management Committee as Resident Surgical Officer at Stockport Infirmary.

Applications, stating age, experience and qualifications, together with the names of 2 referees, to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw Heath, Stockport.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. WYTHENSHAWE HOSPITAL, MANCHESTER, 23. The Board invite applications from registered practitioners for the post of MEDICAL REGISTRAR at the above Hospital.

Applications, stating age, qualifications, present post, experience, and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER. BOOTH HALL CHILDREN'S HOSPITAL, BLACKLEY, MANCHESTER 9. (380 Beds.) Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST, Senior House Officer grade, which will become vacant during August, 1958. The post, which is tenable for 1 year, affords opportunities for training in all branches of pathology. Candidates should have held house appointments, but previous experience in pathology is not essential.

Application form from Group Secretary.

MANCHESTER. BOOTH HALL CHILDREN'S HOSPITAL, BLACKLEY, MANCHESTER, 9. (380 Beds. Recognised for D.C.H.)

RESIDENT SENIOR HOUSE OFFICER (surgical). Duties orthopædic and E.N.T. Post vacant.

Applications, giving names and addresses of 2 referees, to be sent to Group Secretary, from whom further particulars may be obtained.

HOUSE OFFICER (surgical), pre- or post-registration. Duties mainly general surgery and neurosurgery. Post vacant.

Applications immediately, with usual particulars and copies of 2 recent testimonials, to Group Secretary.

MANCHESTER. NORTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. CRUMPSALL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER in Medicine. Vacant 1st October, 1958.

Applications with names of 2 referees by 25th August, 1958, to Group Secretary, Crumpsall Hospital, Manchester, 8.

MANCHESTER. NORTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. The following Pre-registration HOUSE OFFICER posts are now vacant:—

Ancoats Hospital—surgery and orthopædics.

Manchester Victoria Memorial Jewish Hospital—surgery.

Applications, with names of 2 referees, to the Group Secretary, Crumpsall Hospital, Manchester, 8, by 22nd August, 1958.

MANSFIELD AND DISTRICT HOSPITAL. (205 Beds.) (Recognised training hospital for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (orthopædics) required, with duties in the Casualty Department. Furnished married accommodation available if required. The successful candidate will also be required to undertake services at the Crow Hill Rehabilitation Centre, Debdale Hall, and other hospitals in the Group. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th August, 1958, giving age, nationality, qualifications, present and previous appointments (with dates), naming 3 referees.

MANSFIELD AND DISTRICT HOSPITAL. (205 Beds.) (Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL REGISTRAR required. Duties also at Debdale Recovery Hospital. Furnished married accommodation available if required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th August, 1958, giving age, nationality, qualifications, present and previous appointments (with dates), naming 3 referees.

MEXBOROUGH. MONTAGU HOSPITAL AND ANNEXE. (198 Beds—22 obstetrics, 15 gynæcology.) Locum SENIOR HOUSE OFFICER (obstetrics and gynæcology) required 6th–23rd September, 1958.

Applications to Secretary, Hospital Management Committee, Fern Bank, Doncaster-road, Rotherham.

MEXBOROUGH. MONTAGU HOSPITAL AND ANNEXE. (198 Beds.) Locum SENIOR HOUSE OFFICER (casualty and orthopædics) required.

Applications to the Secretary to the Committee, Fern Bank, Doncaster-road, Rotherham.

NEWCASTLE UPON TYNE. ST. NICHOLAS HOSPITAL, GOSFORTH, NEWCASTLE UPON TYNE, 3. ST. NICHOLAS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (2 years in first instance). This Mental Hospital (1150 Beds) affords opportunities for experience of all modern methods of investigation and treatment. There is an extensive outpatient service, and facilities are given to study for the D.P.M.

Applications, giving details of qualifications and experience, together with names and addresses of 2 referees, to be submitted to the Group Secretary.

NEWCASTLE UPON TYNE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time appointment of REGISTRAR or SENIOR HOUSE OFFICER in the Department of Anæsthetics at the Royal Victoria Infirmary, which is associated with the Medical School of the University of Durham. The post, which is non-resident except for rotational emergency duty, will be for 1 year in the first instance and is subject to the terms and conditions of service of hospital medical staff in the National Health Service. It offers opportunity for study for the F.F.A. R.C.S. examination. Applicants should have held postgraduate appointments in medicine and surgery and should preferably have had some experience in anæsthetics.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE UPON TYNE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time, non-resident appointment of REGISTRAR in the Department of Psychological Medicine at the Royal Victoria Infirmary. Facilities are given to take the Durham D.P.M. course, and duties varied to provide all types of inpatient and outpatient experience, including child psychiatry. The appointment is for 1 year in the first instance and will be subject to Ministry of Health terms and conditions of service for hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

Royal Victoria Infirmary, Newcastle upon Tyne.

NANTWICH. BARONY HOSPITAL. South Cheshire HOSPITAL MANAGEMENT COMMITTEE. Locum JUNIOR HOSPITAL MEDICAL OFFICER (psychiatry) required for holiday 2 weeks, 1st–14th September. Salary as per Whitley Council scale.

Apply immediately, stating age, qualifications, &c., with names of 2 referees, to the Group Secretary, Barony Hospital, Nantwich, Cheshire.

NEWBURY DISTRICT HOSPITAL, Newbury, Berkshire. Locum RESIDENT SURGICAL OFFICER (Senior House Officer grade) required for period 1st–14th September, 1958.

Applications to Secretary.

NEWTON ABBOT HOSPITAL. Resident Senior House SURGEON, Male or Female, required immediately, to act as Casualty Officer and House Surgeon to special departments, together with relief duties. Ability to give outpatient anæsthetics advantageous. Married quarters available.

Applications (quoting reference F.364/41), stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, South Devon.

NORTHAMPTON (near). CREATON HOSPITAL. Applications are invited from suitably qualified medical practitioners for the post of SENIOR HOUSE OFFICER. The Hospital has 138 Beds, and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a major thoracic surgical unit for tuberculosis and non-tuberculous diseases of the chest.

Applications, stating age, experience and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton, within 7 days of the appearance of this advertisement.

NORWICH. NORFOLK AND NORWICH HOSPITAL. Applications are invited for the following appointments :—

ORTHOPÆDIC HOUSE SURGEON. 2 House Officers employed in the Department.

HOUSE SURGEON at the West Norwich Hospital. Post recognised for final F.R.C.S. examination requirements. Duties general surgical, and including burns and plastic work. The beds at this Hospital are under the control of the Consultant Staff of the Norfolk and Norwich Hospital.

Locum SURGICAL REGISTRAR at the West Norwich Hospital, for 3 months from the 24th August, 1958, whilst permanent holder of post is on study leave. Resident or non-resident. Salary £19 5s. per week in accordance with terms and conditions of service of hospital medical staff.

Membership of a Medical Defence Society is a condition of appointment in each case.

Applications, stating age, qualifications, and experience, together with names of 2 referees, to Group Secretary, Hospital Management Committee, St. Stephen's-road, Norwich.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of HOUSE SURGEON, vacant immediately. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications, and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (anæsthetics) required 31st August, 1958. The post is recognised for the D.A. and the F.F.A. R.C.S. This is a busy general hospital giving experience in all branches of surgery.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

OXFORD. WARNEFORD HOSPITAL, WARNEFORD CLINIC, and THE PARK HOSPITAL FOR CHILDREN. SENIOR HOUSE OFFICER required (resident). Warneford Hospital, 72 Beds ; Warneford Clinic (de-designated), 78 Beds ; and Park Hospital for Children, 30 Beds, with outpatient departments, give comprehensive psychiatric experience and training facilties. Accommodation for single person.

Apply before 12th September to the Physician-Superintendent, Warneford Hospital, with names of 2 referees.

OXFORD REGIONAL HOSPITAL BOARD. Registrar in Thoracic Surgery at Peppard Chest Hospital, near Reading, for an initial period of 1 year (236 Beds, including 60 for surgical cases). The special surgical unit contains 34 Beds. Married accommodation available.

Application forms, obtainable from the Secretary, Registrar Committee, 43, Banbury-road, Oxford, should reach him by 30th August, 1958.

OXFORD REGIONAL HOSPITAL BOARD. Registrar in Anæsthetics to the hospitals of the Reading area. The appointment, which is recognised for the F.F.A. R.C.S. diploma, will be for 1 year and eligible for extension to 2 years. Single accommodation is available.

Applications, on forms obtainable from the Secretary, Registrar Committee, 43, Banbury-road, Oxford, should reach him by 30th August, 1958.

OXFORD. UNITED OXFORD HOSPITALS. Oxford REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the post of FIRST ASSISTANT (Senior Registrar) to the Orthopædic and Accident Services in the United Oxford Hospitals, interchangeable with a similar post in the Nuffield Orthopædic Centre, Oxford. Vacant mid-October. The period of tenure will be approximately equally divided between the 2 posts, and the successful candidate may be required to start in either. Candidates should be Fellows of one of the Royal Colleges of Surgeons. Experience in both branches of orthopædics is essential.

Applications, on forms obtainable from the Secretary, Joint Committee for Senior Registrars, 43, Banbury-road, Oxford, should reach him by 30th August, 1958.

PAISLEY HOSPITALS MATERNITY UNIT (Thornhill AND BARSHAW MATERNITY HOSPITALS). HOUSE SURGEON (obstetrics) required for the above Unit.

Applications to Group Medical Superintendent, Royal Alexandra Infirmary, Paisley.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEONS (general) required for above Infirmary. Posts approved for pre-registration practitioners and F.R.C.S.

Applications to Group Medical Superintendent.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, Greenbank-road. HOUSE SURGEON, pre-registration post, vacant immediately.

Apply, with names of 3 referees, also stating age, nationality, qualifications and experience, to the Group Secretary.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. SENIOR HOUSE OFFICER in Anæsthetics, vacant immediately. Recognised for the D.A. and F.F.A. R.C.S.

Applications, with names of 3 referees, to be sent to the Group Secretary, 7, Nelson-gardens, Stoke, Plymouth.

PONTEFRACT GENERAL INFIRMARY. Resident CASUALTY OFFICER required early September. Graded Senior House Officer. Recognised for Fellowship.

Applications to the Secretary, Pontefract and Castleford Hospital Management Committee, Great Northern House, Salter-row, Pontefract, Yorkshire.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

Royal Portsmouth Hospital (104 orthopædic beds)
ORTHOPÆDIC HOUSE OFFICER (pre-registration). Vacant now.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST, St. Mary's Hospital, Milton-road, Portsmouth.

PRESTON ROYAL INFIRMARY. (400 Beds.) Senior HOUSE OFFICER in Orthopædics. Post recognised for F.R.C.S. Post vacant now.

Applications, with names of 2 referees, to Group Secretary, Preston and Chorley Hospital Management Committee, Royal Infirmary, Preston, Lancs.

PRESTON ROYAL INFIRMARY. (400 Beds.) Post- or Pre-registration HOUSE SURGEON. Post vacant mid-August. Recognised for F.R.C.S.

Applications, with names of 2 referees, to Group Secretary, Preston and Chorley Hospital Management Committee, Royal Infirmary, Preston, Lancs.

READING. BATTLE HOSPITAL. (391 Beds.) Reading AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration) required in the Accident and Orthopædic Department. F.R.C.S. recognised. Also casualty duties. Vacant immediately.

Apply, stating age, qualifications with dates, nationality, present post, with copy of recent testimonial, to Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. (337 Beds.) Applications are invited from registered and provisionally registered medical practitioners for the resident post of HOUSE PHYSICIAN in the Pædiatric Department, vacant 1st September, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

READING. ROYAL BERKSHIRE HOSPITAL. Applications are invited from registered and provisionally registered medical practitioners for 2 posts as RESIDENT HOUSE PHYSICIAN, vacant 1st September, 1958, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copies of 2 recent testimonials, to Secretary, Royal Berkshire Hospital, Reading.

RICHMOND, SURREY. ROYAL HOSPITAL. Senior HOUSE OFFICER (resident) for Casualty and Orthopædics required 1st September for busy General Hospital of 121 Beds with full Consultant staff. Recognition being sought for F.R.C.S.

Apply, giving age, qualifications, experience, and names of 2 referees, to the Administrative Officer immediately.

RICHMOND, SURREY. ROYAL HOSPITAL. Senior HOUSE SURGEON (resident) required 1st September for busy General Hospital of 121 Beds with full Consultant staff. Recognition for F.R.C.S. being sought.

Apply, giving age, qualifications, experience, and names of 2 referees, to the Administrative Officer immediately.

RICHMOND, SURREY. ROYAL HOSPITAL. (121 Beds.) SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified and experienced medical officers for the appointment of Full-time RESIDENT REGISTRAR (general surgery) which will become available shortly. Single or married quarters will be available.

Forms of application may be obtained from the Group Secretary (a foolscap stamped addressed envelope to be enclosed), and the completed forms should be returned to the Group Secretary, 35, Coombe-road, Kingston, as soon as possible.

ROCHDALE AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. HOUSE PHYSICIAN required at Birch Hill Hospital. Resident post now available.

Apply at once to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancs.

ROCHDALE AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. HOUSE OFFICER (surgical) required immediately for busy Surgical Unit. Post recognised for F.R.C.S. qualification and offering excellent experience.

Apply at once to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancs.

ROCHDALE. BIRCH HILL HOSPITAL. Senior House OFFICER (pædiatrics), resident. Post vacant in mid-September. Recognised D.C.H.

Apply to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

ROCHFORD, ESSEX. GENERAL HOSPITAL. Locum PATHOLOGICAL REGISTRAR required at the General Hospital, Rochford, on a month-to-month basis. Single accommodation available, if required. Post vacant immediately.

Apply to the Secretary as soon as possible.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (620 Beds.) HOUSE OFFICER (obstetrics) required. Post vacant 16th September, 1958. Recognised for D.Obst.R.C.O.G. The Hospital has 75 maternity beds, a gynæcological ward of 25 Beds, and a premature-baby unit of 8 Cots.

Applications, stating age, &c., to the Secretary by 23rd August, 1958.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) ORTHOPÆDIC HOUSE SURGEON (resident) required in the Orthopædic and Accident Unit. The service consists of 100 Beds equally divided between traumatic surgery and "cold" orthopædics. Post is recognised for pre-registration purposes and for F.R.C.S.

Applications to be sent to Group Secretary, Romford Hospital Management Committee, Oldchurch Hospital, as soon as possible.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. Resident PATHOLOGIST (Senior House Officer grade). This post, which will become vacant on 1st October, 1958, provides valuable experience by rotation through all departments of this large Group Laboratory and is recognised for the purposes of the Diploma in Pathology. Prospective candidates are invited to visit the laboratory.

Applications should be sent with testimonials or the names of 2 referees, before 18th August, 1958, to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROTHERHAM. MOORGATE GENERAL HOSPITAL. (342 Beds, 38 Cots.) Locum SENIOR HOUSE OFFICER (surgery) required.

Applications, stating qualifications, experience, and names of 3 referees, to Secretary to Committee, Fern Bank, Doncaster-road, Rotherham.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance:—

SENIOR REGISTRAR in Anæsthetics based at Stobhill General Hospital, Glasgow.
SENIOR REGISTRAR in Orthopædic Surgery based at the Royal Alexandra Infirmary, Paisley.
REGISTRAR in Medicine based at the Royal Alexandra Infirmary, Paisley.
REGISTRAR in Surgery based at the County Hospital, Stonehouse, Lanarkshire.
REGISTRAR in Surgery based at the Royal Hospital for Sick Children, Glasgow.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 30th August, 1958.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. REGISTRAR in Medicine at the Deaconess Hospital, Edinburgh (25 medical and 10 pædiatric beds), with duties also in Longmore Hospital (16 medical beds). Vacant on 1st October, 1958.

Apply, giving particulars of age, qualifications and previous experience, and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 30th August, 1958.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. REGISTRAR in Department of Surgical Neurology, Edinburgh; at the Royal Infirmary, Edinburgh; and at Bangour Hospital, near Edinburgh.

Apply, giving particulars of age, qualifications and previous experience, and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, within 14 days.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. SENIOR REGISTRAR in Surgery, Royal Infirmary, Edinburgh.

Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 6th September, 1958.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR in General Surgery at Perth Royal Infirmary (255 Beds). 4-room flat may be made available. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 6th September, 1958.

SALFORD ROYAL HOSPITAL. Salford Hospital MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER (Orthopædic and Casualty Departments), resident. The post is recognised for the F.R.C.S., and will be vacant early October. Gives opportunity for Emergency Surgery.

Applications, with copies of 3 recent testimonials, to the Secretary, Salford Royal Hospital, Chapel-street, Salford, 3.

SALISBURY GENERAL HOSPITAL. Orthopædic Department. Applications are invited for the post of SENIOR RESIDENT HOUSE SURGEON or RESIDENT HOUSE SURGEON, vacant 11th September. Appointment recognised for pre-registration candidates, and also Fellowship regulations. Department has over 50 Beds and large outpatient turnover, dealing with fractures and all types of orthopædic surgery.

Applications, stating age, nationality, qualifications and experience, and naming 2 referees, to the Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

SALISBURY GENERAL HOSPITAL. Salisbury Group HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of MEDICAL REGISTRAR at the above Hospital, with effect from 5th November, 1958.

Further details and application forms obtainable from and should be returned to Group Secretary, Odstock Hospital, Salisbury, within 10 days of the appearance of this advertisement.

SCUNTHORPE. WAR MEMORIAL HOSPITAL. (262 Beds.) Immediate vacancies for RESIDENT HOUSE SURGEONS.

(*a*) General surgery and gynæcology—Senior House Officer or pre-registration.

(*b*) General surgery and E.N.T.—pre-registration or Senior House Officer.

Both posts offer splendid opportunities for experience in a modern well-equipped Hospital.

Applications, naming 2 referees, to Group Secretary, Scunthorpe Hospital Management Committee.

SCUNTHORPE. WAR MEMORIAL HOSPITAL. (262 Beds.) Immediate vacancy for Locum RESIDENT HOUSE SURGEON—Senior House Officer grading.

Applications, naming 2 recent referees, to Group Secretary, Scunthorpe Hospital Management Committee.

SHEFFIELD, 5. CITY GENERAL HOSPITAL. Department of Pathology, Area Laboratory. Applications are invited for the appointment of SENIOR HOUSE OFFICER (clinical pathology). Resident accommodation is available and optional. Opportunities for training in morbid anatomy, biochemistry, hæmatology, and bacteriology. The work of this and associated hospitals offers excellent experience to graduates who wish to make pathology their permanent career. The post is recognised for the D.Path.

Apply, giving details of age, qualifications, present and previous appointments (with dates), and the names of 2 persons to whom reference may be made, to the Group Secretary, Nether Edge Hospital, Sheffield, 11.

SHEFFIELD, 5. CITY GENERAL HOSPITAL. (Recognised for M.R.C.O.G.) Applications are invited for the resident post of SENIOR HOUSE OFFICER (gynæcology), vacant 15th October, 1958. Duties divided between units in the charge of Professor of Obstetrics and Gynæcology, University of Sheffield, and full-time Consultant respectively.

Applications, stating full details of age, nationality, qualifications, present and previous appointments with dates, and the names of 2 persons for reference, should be forwarded to the Group Secretary, Lyndhurst, Nether Edge Hospital, Sheffield, 11, by not later than 31st August, 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL INFIRMARY AND CHILDREN'S HOSPITAL. Applications invited for the non-resident post of REGISTRAR in E.N.T. at the above Hospitals. Post vacant 1st October.

Applications, with the names of 3 referees, should be sent not later than 23rd August, 1958, to Chief Administrative Officer, United Sheffield Hospitals, West-street, Sheffield, 1.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE PHYSICIAN/HOUSE SURGEON to run consecutively for a period of 6 months in each post. Posts approved for pre- or post-registration practitioners and F.R.C.S.

Applications to Hospital Secretary, Southlands Hospital, Shoreham-by-Sea. A. V. OAKTON, Group Secretary, Worthing Group Hospital Management Committee.

SHREWSBURY. CROSS HOUSES HOSPITAL. Obstetric HOUSE SURGEON. Pre-registration post. Vacant 1st September, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. SENIOR HOUSE OFFICER (E.N.T.). Duties at E.N.T. Hospital (68 Beds) and Copthorne Hospital (168 Beds). Post recognised for the D.L.O. R.C.S. and F.R.C.S. Vacant immediately.

Applications, with copy testimonials, to the Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE SURGEON. Vacant immediately. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SIDCUP, KENT. QUEEN MARY'S HOSPITAL. 2 Senior HOUSE OFFICERS (casualty and orthopædic) required—1 immediately and 1 in September (15th approximately). The successful candidates will serve 3 months in the Orthopædic Department and 3 months as Casualty Officer. The posts are recognised under the Fellowship regulations as giving the required period of 6 months' casualty training.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, should be sent to the Secretary.

SOUTHAMPTON EYE HOSPITAL. (32 Beds.) Locum RESIDENT SENIOR HOUSE OFFICER required for 5 weeks from 25th August, 1958.

Applications as soon as possible to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (274 Beds) AND SOUTHAMPTON GENERAL HOSPITAL (465 Beds). SENIOR HOUSE OFFICER (E.N.T.) required end of August. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing hearing-aid centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Obstetrics and Gynæcology to fill a vacancy in the approved trainee establishment at the Brighton and Lewes Group of hospitals as from 1st November, 1958. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales) and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications, and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 30th August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Pathology to fill a vacancy in the approved trainee establishment at the Brighton and Lewes Group of hospitals. The post is non-resident, but the successful candidate will be expected to reside near the Royal Sussex County Hospital and to take a share of emergency night duties in the group. This post is recognised for the Diploma in Pathology. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 30th August, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Orthopædic Surgery (resident or non-resident) to fill a vacancy in the approved trainee establishment in the Tunbridge Wells Group of hospitals for duties mainly at Pembury Hospital. There is a wide variety of short- and long-stay work and fractures. The post is recognised for the F.R.C.S. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales) and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 30th August, 1958.

SOUTHEND. GENERAL HOSPITAL. House Surgeon required for General Surgery and E.N.T. Resident post. Some duties at Victoria Hospital, Westcliff.

Applications as soon as possible to the Secretary.

SOUTHEND-ON-SEA. GENERAL HOSPITAL. Locum MEDICAL REGISTRAR required on or about 1st September, 1958, pending appointment being filled by the Regional Hospital Board.

Applications immediately to the Secretary.

SOUTHEND-ON-SEA. GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT ANÆSTHETIST (Senior House Officer grade). Post vacant 1st October, 1958. The appointment is recognised as fulfilling the conditions of the F.F.A. R.C.S. and the D.A.

Applications, stating age, experience, and qualifications, with copies of 2 testimonials, should be sent to the Secretary at the General Hospital, Southend, not later than 28th August, 1958.

SOUTHPORT GENERAL INFIRMARY. (159 Beds. Recognised for pre-registration and F.R.C.S.) HOUSE SURGEON (general surgery and gynæcology). Post vacant now.

Apply, with 2 copy testimonials, to Group Secretary, Southport and District Hospital Management Committee, Promenade Hospital, Southport.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time JUNIOR HOSPITAL MEDICAL OFFICER in the Blood Transfusion Service in the South West and South East Metropolitan Regions. Duties include the collection of blood from donors in area covered by South West and South East Metropolitan Regional Hospital Boards and work in the London laboratories at the South London Blood Transfusion Centre, Stanley-road, Sutton, Surrey. Salary scale: £852 10s.–£55–£1182 10s. p.a.

Applications (2 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 6th September, 1958. Applicants may visit Blood Transfusion Centre by local arrangement.

ST. ALBANS, HERTFORDSHIRE. CELL BARNES HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required at above Hospital. This is a modern Hospital where 895 mental defectives of all types and ages are under care. Approved for D.P.M. Good paediatric experience available. Hospital may be visited by direct appointment.

Application forms obtainable from the Group Secretary, Harperbury Hospital, St. Albans, Hertfordshire, and returnable by 26th August, 1958.

ST. ALBANS, HERTFORDSHIRE. CELL BARNES HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. JUNIOR HOSPITAL MEDICAL OFFICER required at above Hospital. This is a modern Hospital where 895 mental defectives of all types and ages are under care. Approved for D.P.M. Good paediatric experience available. Hospital may be visited by direct appointment.

Application forms obtainable from the Group Secretary, Harperbury Hospital, St. Albans, Herts, and returnable by 26th August, 1958.

ST. ASAPH HOSPITAL, St. Asaph, Flintshire. Appointment of HOUSE OFFICER. Duties divided between ophthalmology (16 Beds), E.N.T. (12 Beds), and oral surgery (4 Beds).

Applications, stating age, qualifications and experience, accompanied by 2 recent testimonials, to be sent forthwith to the Group Secretary, Clwyd and Deeside Hospital Management Committee, "Rhianfa", Russell-road, Rhyl.

ST. HELENS AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. ST. HELENS HOSPITAL. (196 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON, which is recognised for pre-registration service and for the F.R.C.S. examinations. The appointment will be made in the Senior House Officer grade in the case of a candidate who has already held 2 pre-registration posts.

Applications, stating age, date of qualification and experience, and giving 2 names for reference, should be forwarded to N. RICHARDS, Group Secretary, Whiston Hospital, Prescot, Lancs, immediately.

STAFFORD GENERAL INFIRMARY. Senior House OFFICER (anæsthetics) required September. Resident. Post recognised for D.A. examination.

Applications to Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.) Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (Medicine), vacant 18th August, 1958.

Applications, stating age, experience and qualifications, together with copies of 2 testimonials, to be addressed to the Group Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE PHYSICIAN (general medicine and paediatrics) required. Pre-registration post, vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE PHYSICIAN (general medicine and dermatology) required. Pre-registration post. Post vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. Gynæcology Department. SENIOR HOUSE OFFICER required. Post vacant shortly. Recognised for M.R.C.O.G. (surgery). Experience in abnormal obstetrics available, but the work is mainly gynæcological.

Detailed applications, with copy testimonials, to Hospital Secretary.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. (455 Beds.) SENIOR HOUSE OFFICER (orthopædics) required. Post vacant very shortly. Some duties also at Hartshill Orthopædic Hospital.

Detailed applications, with copy testimonials, to Hospital Secretary.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. SENIOR HOUSE OFFICER in General Surgery required—post vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary, Stoke-on-Trent.

SUTTON AND CHEAM HOSPITAL, Cotswold-road, SUTTON, SURREY. RESIDENT SENIOR HOUSE OFFICER (Casualty Officer). Post recognised for F.R.C.S. Vacant 27th August.

Applications, stating age, qualifications and experience, with copies of recent testimonials and the names of 2 referees, to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

SWANSEA HOSPITAL, Swansea. (413 Beds.) GLAMTAWE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER in the Surgical Unit of the above Hospital. The post is recognised under the F.R.C.S. (Eng.) regulations.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, should be forwarded to the Secretary of the Hospital.

T. E. JONES, Group Secretary.

SWINDON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for 2 appointments of SENIOR HOUSE OFFICER as Casualty Officer and Orthopædic House Surgeon at Great Western Hospital, Swindon. Posts recognised by R.C.S. for 6 months of year's training under Fellowship regulations. Work of Accident and Orthopædic Department, associated with Nuffield Orthopædic Centre, Oxford, includes large number of industrial injuries. Salary £819 10s. p.a., less residential emoluments.

Full details and names of 3 referees to Secretary, 7, Okus-road, Swindon, Wilts.

TAUNTON AND SOMERSET HOSPITAL, Taunton, SOMERSET. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty and orthopædic).

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton.

TAUNTON AND SOMERSET HOSPITAL, Taunton, SOMERSET. HOUSE OFFICER (general surgery) required. Pre-registration post recognised for F.R.C.S., vacant now.

Applications, stating age, nationality and qualifications, to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL. (357 staffed available beds.) TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for post of HOUSE PHYSICIAN (Senior House Officer) in Paediatric Unit. Vacant 1st October, 1958. Previous pædiatric experience desirable. Post tenable for 12 months and recognised for D.C.H. examination.

Apply, stating age, qualifications and experience, with 3 recent testimonials, by 30th August, to Group Secretary, Tunbridge Wells Group Hospital Management Committee, Sherwood Park, Pembury-road, Tunbridge Wells.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY, KENT. (357 Beds.) TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for pre-registration post of ORTHOPÆDIC HOUSE SURGEON. 6 months' appointment. Vacant now.

Apply, giving details of age, experience and qualifications, to Surgeon-Superintendent.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY, near TUNBRIDGE WELLS. TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for appointment of SENIOR ORTHOPÆDIC HOUSE SURGEON AND CASUALTY OFFICER (Senior House Officer grade) to begin duties on 1st September, 1958. Recognised for F.R.C.S. (Eng.) and tenable for 1 year. Work includes treatment of long- and short-stay cases and traumatic surgery with large Outpatient and Fracture Clinics under 2 Consultants.

Apply, stating age, qualifications and experience, with 3 testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. (Regional Thoracic Centre.) Applications invited for positions of SENIOR HOUSE PHYSICIAN and SENIOR HOUSE SURGEON. Salary £819 10s. p.a. £150 p.a. charged for accommodation.

Address written applications, giving full personal particulars, details of experience and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WAKEFIELD. STANLEY ROYD HOSPITAL. Applications invited for post of JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER in Psychiatry. Accommodation available for a single person.

Address written applications, giving full personal particulars, details of training, experience, &c., and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the posts of 2 HOUSE SURGEONS at the above Hospital. Pre-registration posts and recognised for F.R.C.S. Salary according to the National Health Service scale.

Applications, with copies of recent testimonials, to the Administrator.

WATFORD. SHRODELLS HOSPITAL. (General Hospital, 366 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to the Geriatric Unit. Resident or non-resident. This unit of 180 Beds, under a full-time Consultant Geriatrician, offers excellent clinical experience in diagnosis and treatment of acute and other illnesses in the elderly. Full laboratory and radiological facilities. Adequate time for reading.

Applications, together with copies of not more than 2 testimonials, should reach the Medical Administrator as soon as possible.

WELSH REGIONAL HOSPITAL BOARD. Registrar (general medicine), based at Caerphilly District Miners' Hospital, Caerphilly. Married quarters may be available outside Hospital. Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens REGISTRAR required, Radiotherapy Centre, Whitchurch Hospital, near Cardiff. Duties of appointment afford experience in general surgery, gynæcology, and radiotherapy.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD.

REGISTRAR in Thoracic Medicine, Llangwyfan Hospital, near Denbigh. Modern methods of treatment of tuberculosis and chest diseases. 370 adult beds (Male and Female) and children. Hospital also contains major thoracic unit. Vacant 7th September, 1958.

REGISTRAR in General Medicine, West Wales General Hospital, Carmarthen (188 Beds). Resident non-resident.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WESTON-SUPER-MARE GENERAL HOSPITAL. (104 Beds.) Applications are invited from duly qualified medical practitioners for the pre-registration appointment (resident) of HOUSE SURGEON. Immediate vacancy.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Group Secretary, Weston-super-Mare Hospital Management Committee.

WALSALL HOSPITAL MANAGEMENT COMMITTEE. Locum HOUSE SURGEON and HOUSE PHYSICIAN required for the General (Sister Dora) Hospital and the Manor Hospital.

Apply Group Secretary, Walsall General (Sister Dora) Hospital.

WARRINGTON GENERAL HOSPITAL. (344 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Male or Female), graded as Senior House Officer. The Hospital is recognised for the D.A. examination. Salary is £819 10s. p.a., less a deduction of £150 p.a. for residential emoluments.

Applications, stating qualifications and experience, should be sent to HENRY L. BOOT, Group Secretary, Warrington and District Hospital Management Committee, c/o General Hospital, Warrington, Lancs.

WHITEHAVEN HOSPITAL, Cumberland. (122 Beds, pre-registration post.) HOUSE PHYSICIAN (first, second or Senior House Officer post). Vacant beginning of October.

Detailed application, with dates and names of 2 referees, to Group Secretary, Workington Infirmary, Cumberland.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE. LEIGH INFIRMARY, LEIGH. SENIOR HOUSE OFFICER required for Casualty Department, with gynæcological and surgical duties at Astley Hospital. Resident post. Vacant now.

Apply Secretary, Knowsley House, Wigan.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE. WHELLEY HOSPITAL. (71 acute medical beds.) HOUSE PHYSICIAN, pre-registration post.

Applications, with names of 2 referees, to Secretary, Knowsley House, Wigan.

WINCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Anæsthetics (Registrar grade) required at the Royal Hampshire County Hospital, Winchester, with duties in the Alton Group. Post recognised for the F.F.A. R.C.S., and is resident or non-resident.

Forms of application obtainable from Group Secretary, Royal Hampshire County Hospital, Winchester.

WINDSOR. KING EDWARD VII HOSPITAL. Locum RESIDENT SENIOR HOUSE OFFICER (casualty) required immediately.

Applications, with names of 2 referees, to Hospital Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. Registrar (Casualty Officer), resident or non-resident, required immediately. There is an accident unit of 30 Beds at the Hospital, and with the Casualty Department forms part of the Accident Service for the Windsor Group and includes duties with the E.N.T. and Eye Departments. Candidates should have had previous experience in the treatment of acute injuries.

Application forms from and returnable to Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor.

WOLVERHAMPTON. NEW CROSS HOSPITAL. Pre-registration HOUSE OFFICER in General Surgery. Post recognised for F.R.C.S.

Applications to Hospital Secretary.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER required (Locum Tenens approximately October–December) for Geriatric Department. Consultant Geriatrician in post with active inpatient treatment and outpatient clinics.

Applications to Group Secretary, The Royal Hospital, Wolverhampton.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) RESIDENT SENIOR HOUSE OFFICER required for Geriatric Department. Consultant Geriatrician in post with active inpatient treatment and outpatient clinics.

Applications to Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An associated hospital of the Birmingham University Medical School.) HOUSE OFFICER (pre-registration) E.N.T. Department. Post recognised for the D.L.O. and F.R.C.S. examinations. Vacant 10th September.

Apply, with copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. Senior HOUSE SURGEON for Thoracic Surgery and Casualty. Post recognised for F.R.C.S. Vacant immediately.

Apply, with 2 testimonials, to Secretary.

WORTHING HOSPITAL, Lyndhurst-road, Worthing, SUSSEX. (210 Beds. Acute general.) The post of HOUSE SURGEON is vacant immediately.

Applications from either registered medical practitioners or pre-registration candidates, stating age, qualifications, experience, nationality and enclosing copies of 2 recent testimonials, to be forwarded to the Hospital Secretary immediately.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

WREXHAM. MAELOR GENERAL HOSPITAL (591 Beds) AND WAR MEMORIAL HOSPITAL, WREXHAM (230 Beds). Applications are invited for HOUSE PHYSICIAN and SURGEON posts at the above Hospitals to commence immediately. The appointments are recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Wrexham, Denbighshire.

WREXHAM. MAELOR GENERAL HOSPITAL. (591 Beds.) Applications are invited for the post of PÆDIATRIC HOUSE PHYSICIAN at the above Hospital, to commence immediately. The appointment is recognised for the D.C.H. and for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Wrexham, Denbighshire.

WORKINGTON INFIRMARY, Cumberland. (174 Beds, pre-registration post.) HOUSE OFFICER, obstetrical and gynæcological (House Officer or Senior House Officer grade). Vacant beginning of October.

Detailed application, with dates and names of 2 referees, to Secretary.

YORK A AND TADCASTER HOSPITAL MANAGE-MENT COMMITTEE. YORK MILITARY HOSPITAL (Civilian Wing). (60 Beds.) SENIOR HOUSE OFFICER required immediately. There are 30 general medical beds and 30 surgical beds. The Hospital is associated with the County Hospital, a general hospital of 266 Beds, where relief casualty and emergency work and relief work for House Surgeons may be undertaken and where residence can be provided. Applicants may be resident or non-resident.

Applications, stating age, nationality, experience, qualifications and names of 2 referees, to Group Secretary, Bootham Park, York.

YORK. CITY HOSPITAL. (General—256 Beds.) Locum Tenens JUNIOR HOSPITAL MEDICAL OFFICER required in Casualty Department from 8th to 28th September inclusive.

Applications, stating age, experience, qualifications, and the names of 2 referees, to Group Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

YORK. THE RETREAT. Applications are invited for the post of REGISTRAR in Psychiatry (Male or Female). Facilities are available for attendance at the D.P.M. course at Leeds University. Accommodation for single person if required. Salary as in National Health Service scale. Superannuation is transferable to and from the National Health Service.

Applications, with names of 2 referees, should be sent to the Physician-Superintendent, The Retreat, York, within 2 weeks of the appearance of this advertisement.

CHANNEL ISLANDS. JERSEY GENERAL HOSPITAL. (200 Beds—D.A. recognised.) Applications are invited for the position of RESIDENT SENIOR HOUSE OFFICER for anæsthetic duties. The post falls vacant on 25th September, 1958. The appointment is for 12 months in the first instance. Salary £850 p.a., less £125 for residential emoluments.

Applications to be submitted not later than 27th August, 1958, to the President, Public Health Committee, General Hospital, Jersey, C.I.

AUSTRALIA. GIPPSLAND BASE HOSPITAL, City of SALE, VICTORIA, AUSTRALIA. Vacancies exist for the appointment of 2 fully registered JUNIOR MEDICAL OFFICERS in this regional hospital. Training facilities available in medicine, surgery, midwifery, gynæcology and pædiatrics. Salary to commence £800 sterling rising in 2 annual increments of £100 sterling. Contract for 3 years initially with possibilities of extension. Free residential emoluments for single and married applicants with married quarters available. Excellent opportunities in general practice.

Applications and inquiries directed to E. C. SPEECHLEY, Secretary and Superintendent.

Public Appointments

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
KINGTON ..	.. HEREFORD..	.. 30TH AUGUST, 1958
CARLUKE ..	.. LANARK ..	.. 30TH AUGUST, 1958

BIRMINGHAM. CITY OF BIRMINGHAM EDUCATION COMMITTEE. Applications are invited from registered medical practitioners (Men or Women) for appointment as SCHOOL MEDICAL OFFICER in the School Health Service. The possession of a D.P.H. or D.C.H. will be an advantage. Salary in accordance with Whitley Council scale of £1050–£50–£1200–£55–£1475 p.a. Appointment is subject to the appropriate superannuation Act and to the passing of a medical examination.

Forms of application obtainable from the undersigned (stamped addressed envelope) must be returned not later than Monday, 1st September. Canvassing disqualifies.

E. L. RUSSELL, Chief Education Officer.
School Health Service,
102, Edmund-street, Birmingham, 3.

CAMBRIDGESHIRE COUNTY COUNCIL. Applications are invited for the post of COUNTY MEDICAL OFFICER OF HEALTH for the Administrative County of Cambridge from men of not more than 50 years of age who are duly qualified medical practitioners registered in the medical register as holders of a diploma in sanitary science, public health or state medicine. The salary offered is £2500–£105(2)–£55(1)–£2765 p.a., and the post is designated for purposes of superannuation subject to the successful candidate passing a medical examination.

Further particulars and a form of application can be obtained from the Clerk of the Cambridgeshire County Council, Shire Hall, Cambridge. Applications must be received not later than Saturday, 20th September, 1958.

NATIONAL COAL BOARD. EAST MIDLANDS DIVI-SION. Applications are invited from registered medical practitioners for the post of MEDICAL OFFICER, based on a static X-ray Unit at Bulwell, Nottingham. The successful candidate will be responsible for the radiological service in the Division. He will also have some opportunity to familiarise himself with the practice of industrial medicine. Some travelling to collieries will be involved. Previous experience of chest disease and/or radiology will be an advantage, though training in the diagnosis of industrial pulmonary disease will be given. Salary, according to qualifications and experience, within the range £1600–£2400 with superannuation.

Applications, giving age and full details of qualifications, experience (with posts held), present post and salary, to Staff Director, National Coal Board, East Midlands Division, Sherwood Lodge, Arnold, Nottingham, quoting S.V. 892.

EAST HERTFORDSHIRE COMBINED SANITARY DISTRICT. Applications are invited from registered medical practitioners having the qualifications set out in the Sanitary Officers' (Outside London) Regulations, 1935, for the appointment of MEDICAL OFFICER OF HEALTH of the East Hertfordshire Combined Sanitary District, which comprises the Borough of Hertford, the Urban Districts of Hoddesdon, Sawbridgeworth, and Ware, and the Rural Districts of Braughing and Ware, having a total area of approximately 87,020 acres, and a population of about 66,490. The commencing salary will be £1740 p.a. plus £100 p.a. in respect of the combined districts, rising by 4 annual increments of £55 to a maximum total salary of £2060. The successful applicant will be required to use his own car, for which an allowance based on the essential users' scale, limited to 10 h.p. or 1199 c.c., will be paid. The person appointed will be required to perform all the duties of a Medical Officer of Health, as defined by the orders from time to time made by the Minister of Health, to devote his whole time to the duties of his office, not to engage in private practice, and to reside as soon as practicable within the district.

Applications, stating age, qualifications, experience, and date upon which duties can be commenced, together with the names and addresses of 3 persons to whom reference can be made, must be delivered to the undersigned on or before Saturday, 30th August, 1958. Canvassing, either directly or indirectly, will disqualify, and applicants must state whether or not they are related to any member of, or the holder of, any senior office under the above authorities.

LESLIE G. SOUTHALL, Clerk of the Joint Committee.
Council Offices, The Priory, Ware, Herts. August, 1958.

MANCHESTER. CITY OF MANCHESTER. Health DEPARTMENT. Applications are invited from registered medical practitioners (Male or Female) for the position of MEDICAL OFFICER (Maternity and Child Welfare) on the permanent staff. Applicants should have obstetric and paediatric experience and will be required to undertake duties principally in Maternity and Child Welfare Clinics. Possession of the D.Obst.R.C.O.G., D.P.H., or D.C.H. will be an advantage. Salary scale £1050 rising to £1475 p.a., the commencing salary depending on previous experience, Medical Council "C" conditions of service.

Application forms may be obtained from the Town Clerk, Town Hall, Manchester, 2, to whom they should be returned within 21 days of the appearance of this advertisement.

NORTH WESTERN GAS BOARD. Applications are invited for the pensionable appointment of MEDICAL OFFICER. The successful candidate will work under the direction of the Chief Medical Officer. The commencing salary will be £1600 p.a.

Further details may be obtained on application. Detailed applications, giving the names of 2 referees, should reach the Secretary, North Western Gas Board, 60, Whitworth-street, Manchester, 1, within 21 days.

NOTTINGHAM. CITY OF NOTTINGHAM. Health SERVICES. Applications invited for appointment of ASSISTANT MEDICAL OFFICER OF HEALTH for general duties including maternal and child health and immunisation. Possession of the D.P.H. an advantage. Post superannuable subject to medical examination. Salary £1050–£1475 p.a. Commencing salary according to local government experience.

Application forms to be obtained from Medical Officer of Health, Huntingdon-street, Nottingham, and to be returned to him by 2nd September, 1958. T. J. OWEN, Town Clerk.

STOKE-ON-TRENT. CITY OF STOKE-ON-TRENT. PUBLIC HEALTH DEPARTMENT. Applications are invited from qualified medical practitioners for the post of ASSISTANT MEDICAL OFFICER on the Maternity and Child Welfare Services. Candidates should have experience in diseases of children and obstetrics. Opportunity will be given for hospital contact with both paediatrics and obstetrics. The possession of a D.P.H., D.C.H., or D.Obst.R.C.O.G. will be considered an additional qualification. The salary will be at the rate recommended by the Whitley Council, with starting salary according to experience. The appointment will be subject to the provisions of the National Health Services (superannuation) regulations, 1947, and the successful candidate will be required to pass a medical examination.

Forms of application may be obtained from the Medical Officer of Health, Public Health Department, Glebe-street, Stoke-on-Trent, and should be returned, accompanied by copies of not more than 3 recent testimonials.

HARRY TAYLOR, Town Clerk.

FEDERAL ARMY OF RHODESIA AND NYASALAND. Applications are invited for appointment as Full-time MEDICAL OFFICERS in the Rhodesia and Nyasaland Medical Corps. Successful applicants (preferably single, age-limit 35) will be required to attest in, and serve as, regular officers in the Corps. Appointments are in the rank of Captain on scale £1371 p.a.–£1899 p.a. In addition to the foregoing, a professional allowance of £200 p.a. will be paid. Promotion in accordance with the requirements of the Service.

Applications should be addressed to the Federal Military Liaison Officer, Rhodesia House, 429, Strand, London, W.C.2, who will arrange an appointment to discuss the career offered.

GOVERNMENT OF BAHRAIN. Medical Department, BAHRAIN, PERSIAN GULF. The Government of Bahrain invites applications from British lady doctors (age 35–45 years) for the post of ASSISTANT to the Senior Lady Medical Officer. Duties will be general and administrative in a new women's hospital of 210 Beds and other medical units. Preference will be given to an M.R.C.O.G. and interest in midwifery. Salary will range from £1800 to £2520 a year (R.2000 to R.2800 a month) depending on experience and degrees. Annual increments of £90. No allowances. No income-tax, provident fund or pension. Free quarters with hard furniture and transport. Agreement for 2 years, renewable, with 5 months' home leave on full pay and air tourist passages. Appointment from November, 1958.

Write to the Crown Agents, 4, Millbank, London, S.W.1. State age, name in block letters, full qualifications and experience, and quote M3C/44916/LD and enclose photograph.

General Practice

For an ***Executive Council post*** *(England and Wales) apply on form* **E.C.16A** *obtainable from the council. Mark envelope "Vacancy."*

COUNTY OF CAITHNESS EXECUTIVE COUNCIL. BURGH OF THURSO, CAITHNESS. Applications are invited from DOCTORS to join the Medical List of the County of Caithness in order to undertake general medical services in the Burgh of Thurso where, owing to expansion of population, additional medical strength is necessary. The successful applicant will be required to provide house and surgery accommodation. An initial practice allowance will be available provided the conditions governing payment are satisfied. Further particulars may be obtained on request, and applications (on Form E.C.16A) should reach the undersigned not later than 30th August, 1958. Applications should be supported with details of professional experience, age, and other relevant particulars.

JAMES CAMPBELL, Clerk, Caithness Executive Council.
Bridge-street, Wick.

EXECUTIVE COUNCIL FOR THE COUNTY OF SURREY. BOROUGH OF MITCHAM. Applications invited for VACANCY which will arise on 1st November, 1958, in above Borough ("Intermediate"). List about 2700 including approximately 170 in London and Croydon. Retiring doctor's residence and surgery available for purchase. Applications on Form E.C.16A to reach the undersigned not later than 3rd September, 1958.

S. H. BENNETT,
Clerk of the Council, Surrey Executive Council.
187, Ewell-road, Surbiton, Surrey.

LIVERPOOL. Childwall Valley. Applications invited in connection with the establishment of a medical practice on a Corporation Housing Estate. There is no list of patients. Accommodation on the Estate will be available. Apply on Form E.C.16A to the undersigned not later than Saturday, 23rd August, 1958.

J. G. DONCASTER, Clerk, Liverpool Executive Council.
36, Princes-road, Liverpool, 8.

OXFORD COUNTY AND CITY. Applications invited for VACANCY (small Rural practice situated North Oxfordshire (near Banbury)). List at present approximately 1062; of these 1032 are dispensing patients. Practice suited to a doctor already established in single-handed practice requiring smaller list. Residence/surgery likely to be available. Apply on Form E.C.16A to the undersigned, not later than 23rd August, 1958.

V. R. PARRY, Clerk of the Council.
73, George-street, Oxford.

Married Assistant required by Partnership of 3 Doctors in a West Midland town. Possible view. Car owner. Start 1st October. Salary and allowances by arrangement.—Address, No. 421, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Miscellaneous

BRITISH GUIANA SUGAR PRODUCERS' ASSOCIATION have 2 vacancies for MEDICAL OFFICERS on their sugar estates starting 1st October.

(1) A temporary appointment on a single 2-year contract.

(2) A permanent appointment, including a good contributory pension scheme, with 3-year tours of service in British Guiana.

Free living quarters, with basic furniture. Car allowance. U.K. leave at the rate of 1 month for every year served overseas. Passages paid both ways for doctor, wife, and children under 16. Minimum starting salary £1500.

Apply, in writing only, giving full details of qualifications and experience, and stating which post is applied for, to: The Medical Officer, BOOKER BROTHERS MCCONNELL AND CO., LTD., Bucklersbury House, 83, Cannon-street, London, E.C.4.

Dr. Barnardo's Homes. Experienced Christian Male Doctor required from 1st October, 1958, as Medical Superintendent at The Village Home, Barkingside. Experience with physically handicapped children desirable. Salary scale £1100–£1500. Apply Chief Medical Officer, 18, Stepney Causeway, London, E.1.

Doctors required to do night calls on a payment-per-call basis, car and medical equipment provided. Excellent opportunity to gain valuable experience in a well-remunerated and congenial appointment.—Please ring REN. 6411 for appointment for interview.

Hamblin Lister-Morton Ophthalmoscope for sale. £16. Address, No. 420, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC. 0141), who are specialists.

Microscopes. Highest prices paid for good modern types. Send or bring your equipment for valuation.—WALLACE HEATON LTD., 127, New Bond-street, W.1.

Hypnotism. Will all doctors interested in this subject for Medical purposes please write to the Secretary, British Society of Medical Hypnotists, 126, Harley-street, W.1.

PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.
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ENTIRELY NEW APPROACH

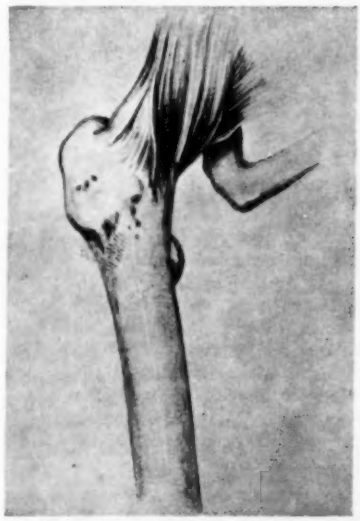
CHRONIC RHEUMATIC DISEASES INVOLVE BOTH MUSCLES AND JOINTS

CODELPRONE

Trade Mark

(Multiple Compressed Tablets, Buffered Prednisolone with Meprobamate)

relieves BOTH joint inflammation and muscle spasm



'Codelprone' gives rapid relief from joint pain and stiffness, shortens the period of disability, and may reduce the incidence of permanent crippling deformity. Since 'Codelprone' contains both prednisolone and meprobamate it represents an **entirely new approach** to the treatment of chronic inflammatory diseases of muscle, tendons and joints.

Some Indications:

Rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, synovitis, tenosynovitis, acute and chronic fibrositis, and certain allergic diseases where a prolonged, low dose of a steroid is required.

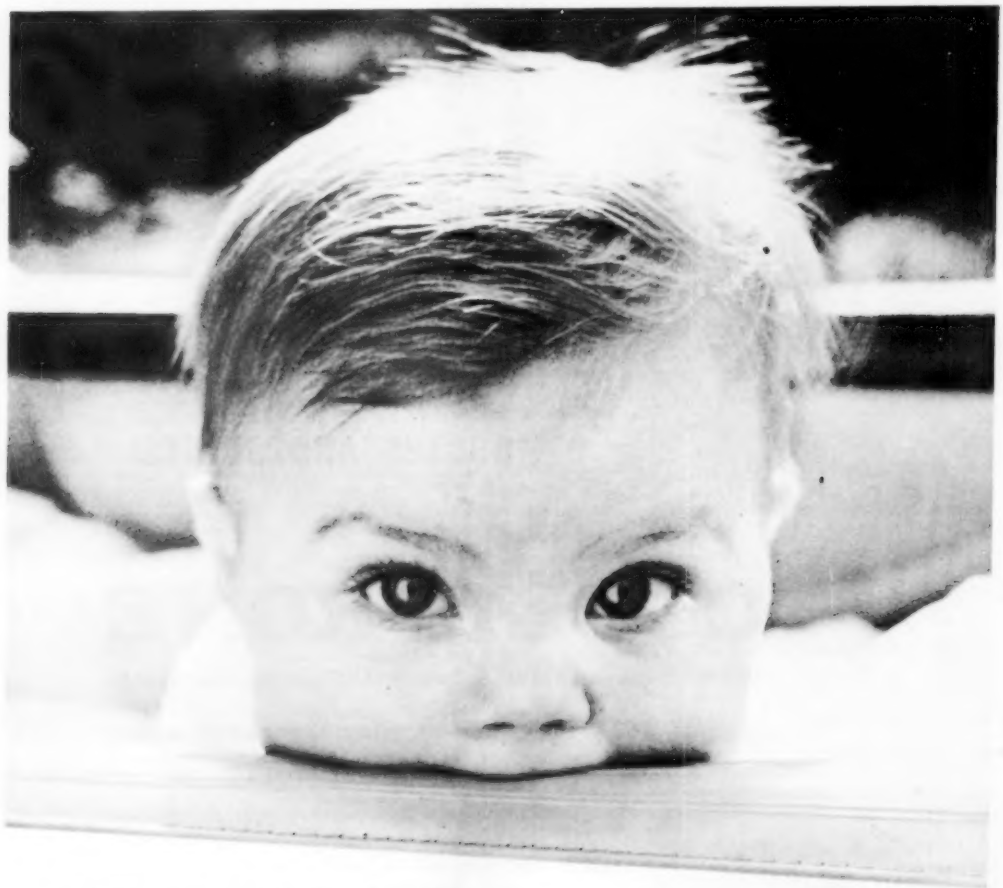
Composition

Each multiple compressed tablet contains: prednisolone 2 mg., meprobamate 200 mg., dried aluminium hydroxide gel 200 mg.

The basic N.H.S. cost of 21 tablets (average week's maintenance therapy) is 15/2d.

Literature gladly supplied on request.

MSD **MERCK SHARP & DOHME LIMITED, HODDESDON, HERTS.**



Kiddies need no coaxing with this new form of Achromycin V

Here's an entirely new form of ACHROMYCIN V especially designed to simplify the control of infection in children and infants. ACHROMYCIN V Pediatric Drops Aqueous—delightfully flavoured with orange—make a particular appeal to the child who turns awkward when it's time to take his medicine.

The product contains ACHROMYCIN tetracycline with citric acid and sodium citrate for more rapid absorption and higher levels of the antibiotic in the blood.

Thus infection can be promptly controlled and the child's recovery accelerated. Accurate dosage can be measured drop by drop from the pliable plastic bottle (5 mg. of tetracycline per drop). The product can be given directly onto the tongue or added to water or fruit juice.

ACHROMYCIN V*

TETRACYCLINE WITH CITRIC ACID AND SODIUM CITRATE

* REGD. TRADEMARK

PEDIATRIC DROPS AQUEOUS

Supplied in dropper-type plastic bottles of 10 cc.

Lederle LEDERLE LABORATORIES DIVISION *Cyanamid* OF GREAT BRITAIN LTD., London, W.C.2